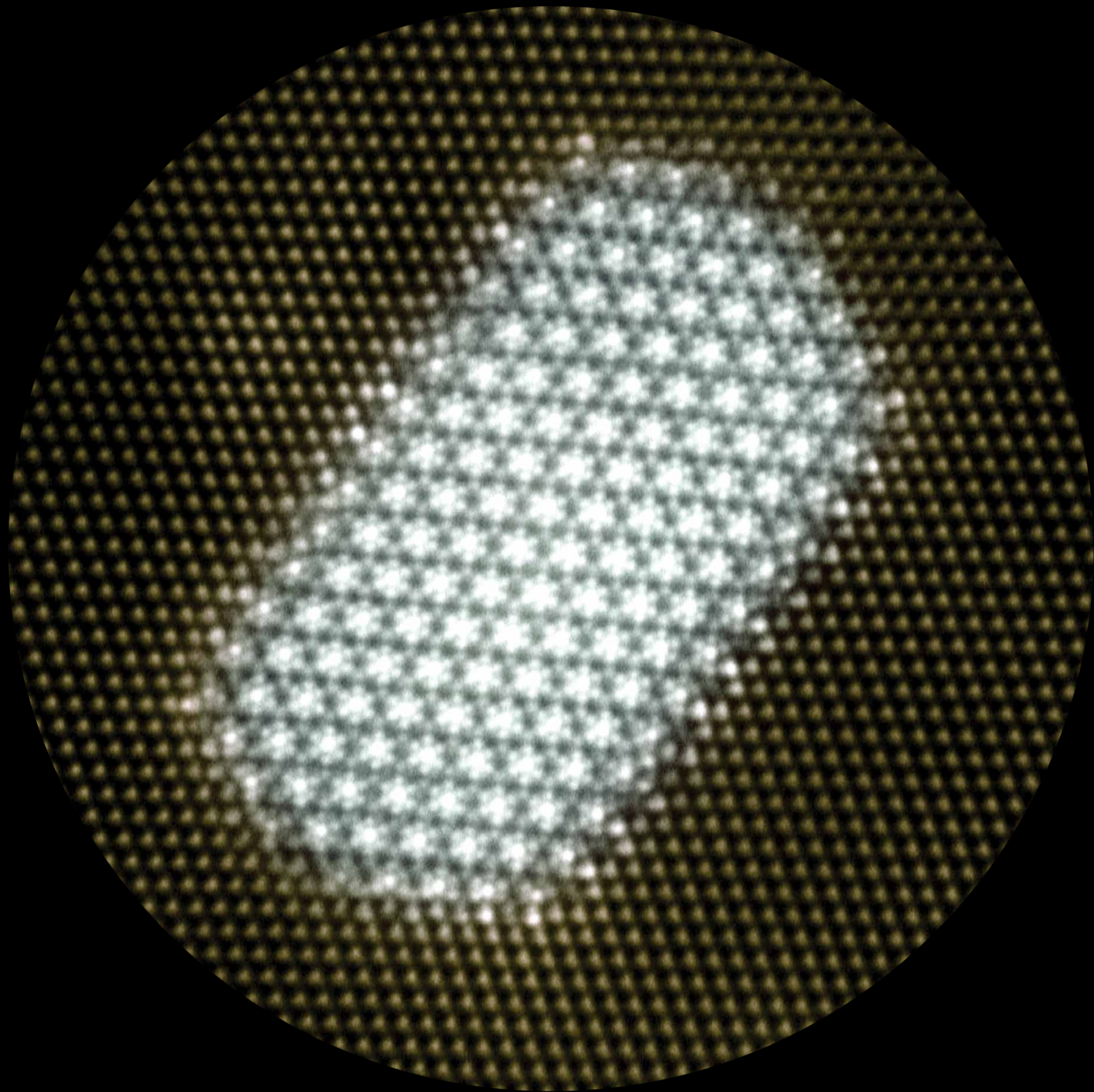
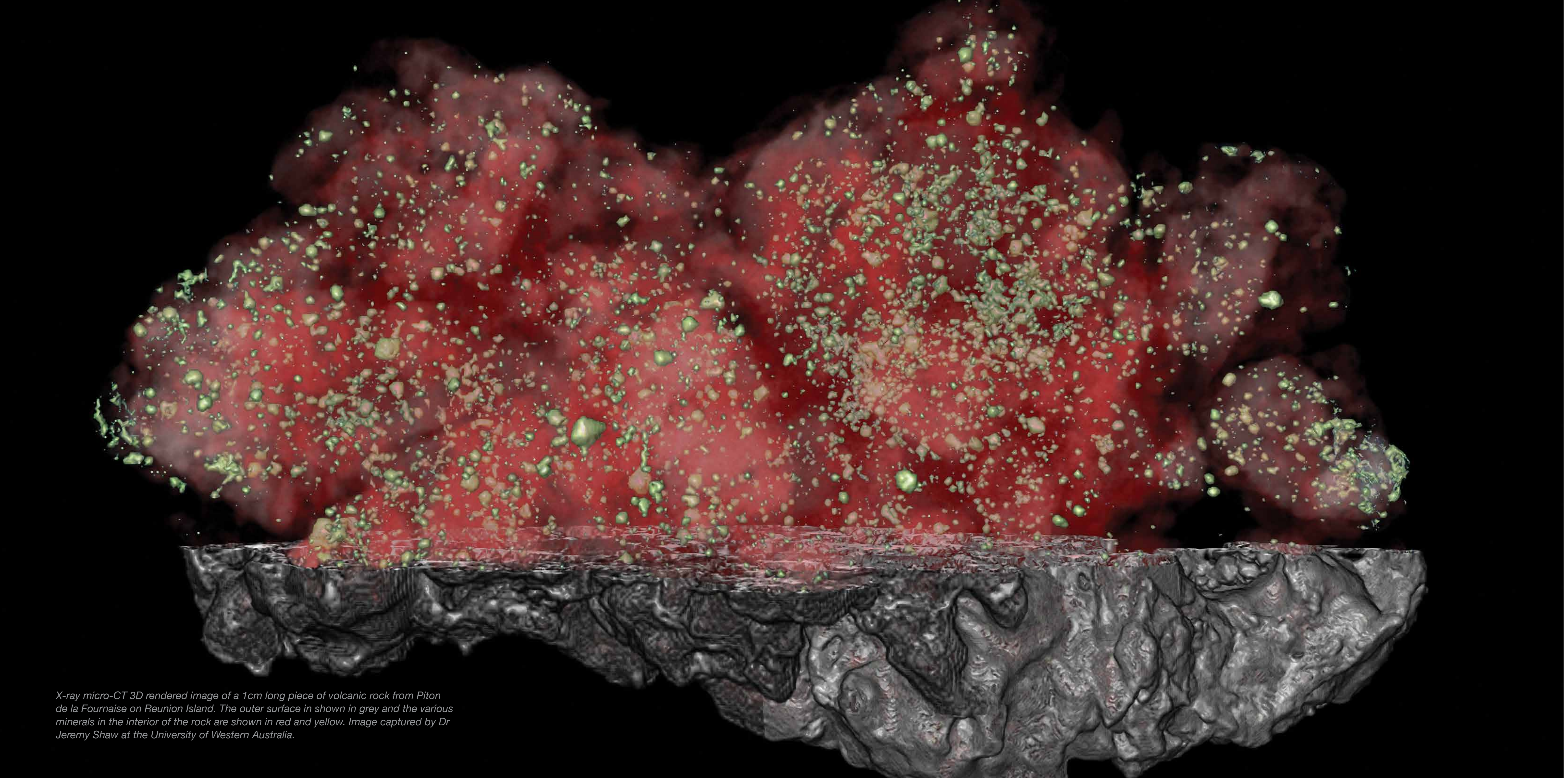
MICROSCOPY AUSTRALIA
RESEARCH HIGHLIGHTS 2019





X-ray micro-CT 3D rendered image of a 1cm long piece of volcanic rock from Piton de la Fournaise on Reunion Island. The outer surface in shown in grey and the various minerals in the interior of the rock are shown in red and yellow. Image captured by Dr Jeremy Shaw at the University of Western Australia.

We invite you to explore how our collaborative research infrastructure empowers discovery and innovation. See how this new knowledge can deliver a healthier and more prosperous Australia.

CONTENTS

Cover image: 'Engineering at the nanoscale'—nanoscale precipitate in an advanced experimental aluminium alloy—from the research of Li Liu, Keita Nomoto, and Simon Ringer (recorded using scanning transmission electron microscopy.

NEWS FROM THE TEAM

MINISTER

Senator the Hon. Dan Tehan,
Minister for Education

Congratulations on another productive year full of achievements.

Microscopy Australia's work is vital in keeping our economy strong, creating jobs and driving innovation, particularly as we strive to create 1.25 million jobs across Australia over the next five years.

Each year, more than 3,500 researchers from universities and industry use Microscopy Australia instruments and expertise around Australia. More than 150,000 trainee microscopists use your training tools around the world every year.

You are empowering and enabling valuable research in areas of national importance including medicine, engineering and agriculture, that will result in economic, environmental, social and health benefits.

This influence and impact will only grow as you continue to increase your presence across Australia, and your expansion into Victoria, through Monash University, will ensure even more researchers have access to your world-class infrastructure.

I wish you continued success next year.

CHAIR

Dr Gregory R. Smith
Chair of Board

Microscopy Australia has expanded. It now operates across nine Australian university facilities. Each facility invests in an overlapping set of expertise, microscopy instrumentation and technologies. This coordinated, collaborative national model continues to optimise capital utilisation and productivity of microscopy-based research for Australia.

After the current round of NCRIS funding was announced in May 2018, the Board is pleased that Microscopy Australia was able to successfully expand into Victoria, adding Monash University to this NCRIS capability.

Microscopy Australia's international standing was reinforced at its annual Scientific Advisory Committee (SAC) meeting, held while at the US Microscopy and Microanalysis conference in Portland, Oregon, last August. SAC attendees highlighted trends including emerging and new microscopy equipment and techniques, computational and software enhancement for data analysis, microscopy automation and remote access, and best practice. Microscopy leaders from USA and Europe expressed their strong interest in increasing interactions with Microscopy Australia.

The Board wants to formally acknowledge the essential support provided by a team of world-class platform engineers who work across Microscopy Australia's facilities. During the year, a new internal professional development program was launched. The "Microscopy Australia Staff Shadowing Scheme", was inspired by a staff shadowing program that has operated within Global BioImaging (GBI). The program provides facility staff with opportunities to learn best practice and different operating models during brief, but intensive, secondments.

This year, attracting the required co-investment from Australian state governments has been a high priority. This will enable us to deliver Microscopy Australia's Five-Year Plan. Co-investment by SA and WA has been secured, with QLD nearing finalisation. Future partnership arrangements with Victoria and NSW are likely to progress in 2020.

The Board is also looking forward to the installation of new, mission critical instruments and research expertise. This national capability enhancement, enabled by NCRIS, will permit Australian researchers and industry clients to continue to achieve results at the leading edge of research and technology.

CEO

Prof. Julie Cairney
Chief Executive Officer

A focus for Microscopy Australia in 2019 has been on implementing our investment plan in response to the 2016 National Research Infrastructure Roadmap. With the release of federal funding in 2018, we have been working with our partners at Universities and State Governments and are proceeding with a number of major capital investments across the country.

As a part of this plan, we officially welcomed Monash University into Microscopy Australia. The Monash Microscopy Australia facilities include the Monash Centre for Electron Microscopy and the Monash Ramaciotti Centre for Cryo-Electron Microscopy. This is a major milestone for us and provides researchers with world-class facilities in Victoria through our open access model. Monash is known for its expertise in transmission electron microscopy for both materials and biological sciences.

Transmission electron microscopy is an important technique area for our users and one that we are expanding. Indeed, there are some fascinating features and stories in this report highlighting a selection of the great outcomes from our existing and newly acquired TEMs. The atomic resolution that they are able to achieve is truly astonishing.

In preparing this annual profile, it is always gratifying to review how Microscopy Australia contributes to Australia's productivity. Over 45% of our users report that their research is directly aligned with industry. We also support almost 100 direct industry clients. This year, in partnership with MTP Connect, we have supported small businesses that might not otherwise have been able to benefit so extensively from our facilities. For example, WearOptimo, who are producing wearable medical devices; and Linear, who are using our facilities for clinical trials that will bring new drugs to market.

As always, our Research Highlights booklet demonstrates the breadth of research we enable and some of the great new knowledge that is generated.

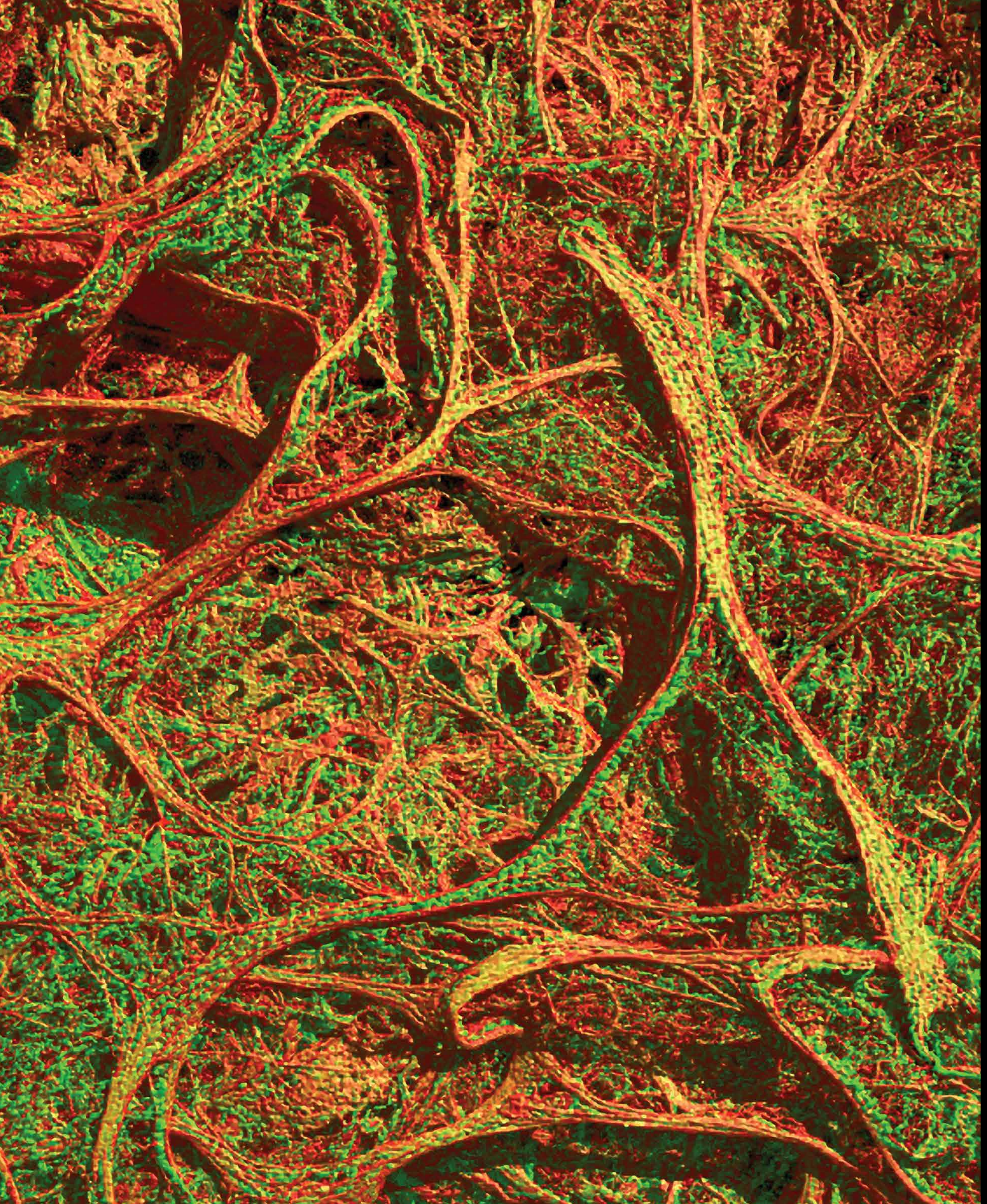


Image: Confocal image of elastin fibres in the lung. Howard Vindin.

STATS

245
INSTRUMENTS

3,154
USERS

99
INDUSTRY CLIENTS

244,021
HRS BEAMTIME

160,000
MYSCOPE USERS

1,359
PUBLICATIONS

48% PHYSICAL & MATERIALS
37% BIOMEDICAL
15% GEOSCIENCE & ENVIRONMENT

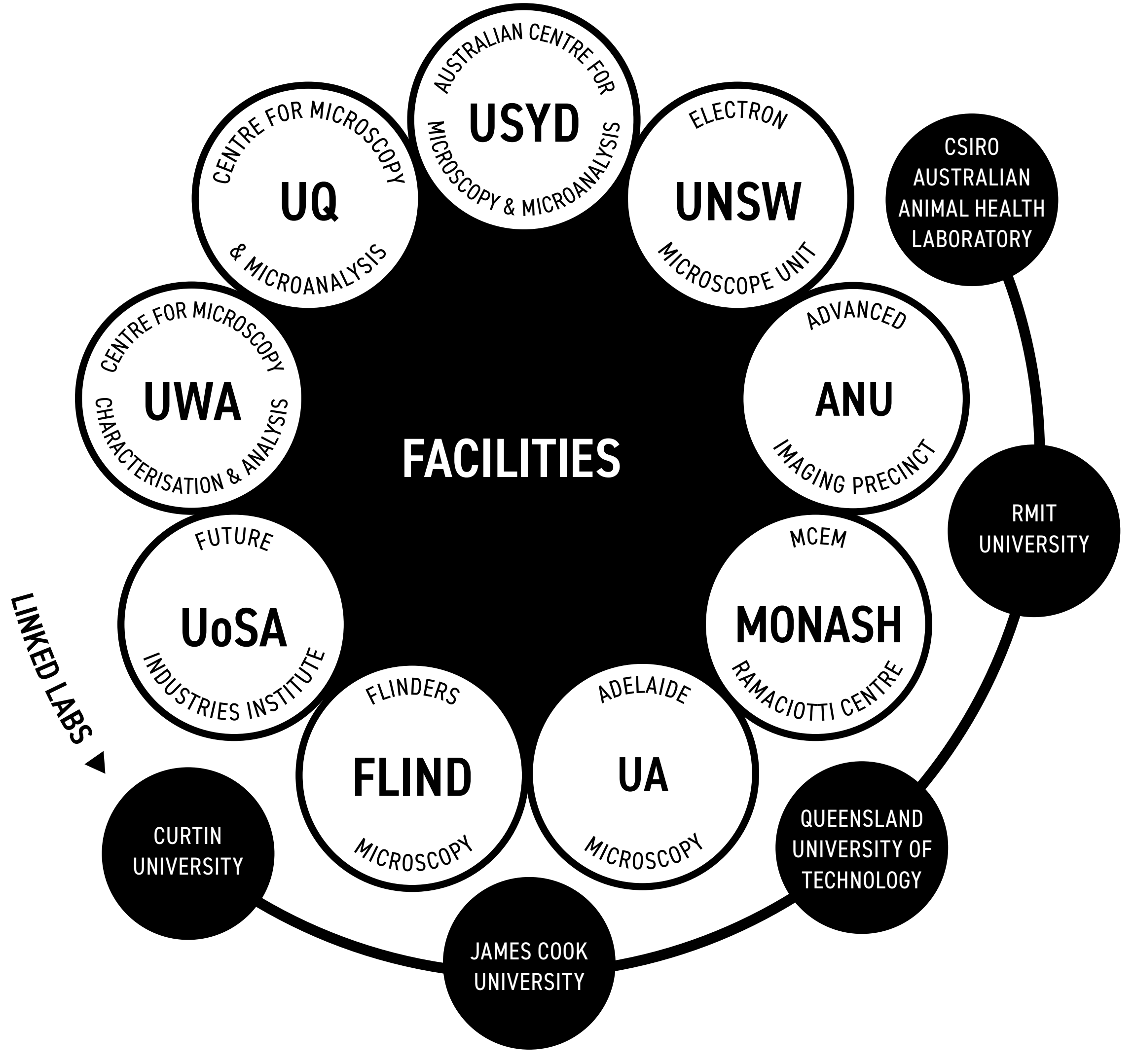
54% MANUFACTURING
18% BIOMEDICAL
28% RESOURCES & ENVIRONMENT

2019

This year's standout achievements include:

- Brought the Monash electron microscopy facilities into Microscopy Australia.
- Secured $8.2M state government co-investment.
- New website launched – see micro.org.au
- Great results coming from our new instruments.
- 98% of our users would recommend our facilities to a colleague.
- 42% publications are in the top 10% most cited journals.
- 37% publications are in top 10% most highly ranked journals.
- Staff shadowing program continues to support professional development – 9 staff awarded funding.
- Continue to enable great research – see some of the highlights from p20.

NETWORK



WELCOME MONASH

The electron microscopy facilities at Monash University are now part of Microscopy Australia

This exciting expansion brings more high-end TEM, SEM and FIB instruments and expertise to Australian researchers through Microscopy Australia's open access model. It also gives us an important world-leading facility in Victoria, where there is such a vibrant research scene. The Monash staff also enrich our community of experts and bring new knowledge for us all to share and pass on to the researchers we support.

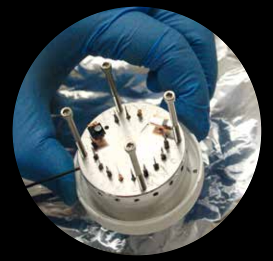
Monash are renowned for their double-aberration corrected TEM and their top-of-the-range cryo-TEM for structural biology. See more about these technologies on page 10.

EQUIPMENT AND EXPERTISE

Microscopy Australia empowers research by providing open access to sophisticated instruments and expertise for researchers around the country. Our dedicated staff ensure that researchers collect high quality data. Our range of specialised techniques is summarised here.

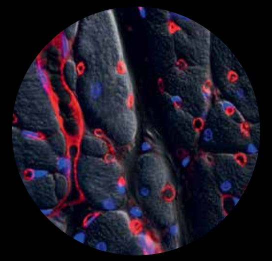
Our online microscopy training tools are also openly accessible with over 160,000 users worldwide in the last year alone.

With the nation's largest range of high-end microscopes and specialists, we also support business across a wide range of industry sectors. Companies of all sizes, from start-ups to multi-nationals, benefit from our services, training and R&D partnerships.



SPECIMEN PREPARATION

Biological & Materials
Cell Culturing & Molecular Preparation
Thermomechanical Processing
Ion Milling & Machining
Ion Implantation

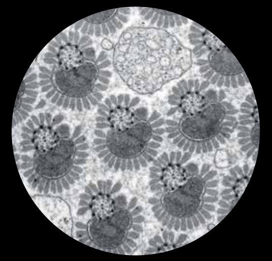


LIGHT & LASER TECHNIQUES

Fluorescence, Confocal & Multiphoton Microscopy
Super Resolution Microscopy
Analytical Spectroscopy
Flow Cytometry
Laser Microdissection

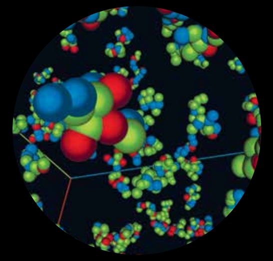
SCANNING ELECTRON MICROSCOPY

Imaging & Analytical Spectroscopy
In-situ Imaging & Testing
Cathodoluminescence
Electron Backscatter Diffraction



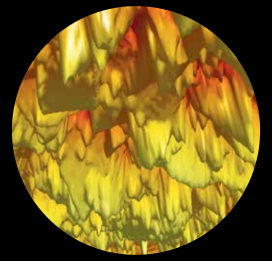
TRANSMISSION ELECTRON MICROSCOPY

Imaging & Analytical Spectroscopy
Cryo-techniques & Tomography
Phase & Z-contrast Imaging
Electron Diffraction



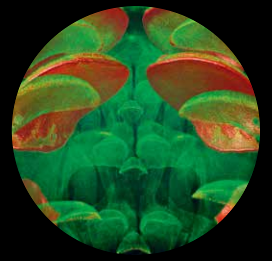
ION & SPECTROSCOPY PLATFORMS

Secondary Ion Mass Spectroscopy
Imaging Mass Spectroscopy
Atom Probe
LA-ICP-MS



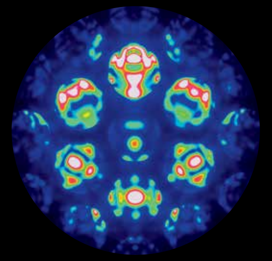
SCANNED PROBE TECHNIQUES

Atomic Force Microscopy
Scanning Tunneling Microscopy
Near-field Scanning Optical Microscopy



X-RAY TECHNOLOGIES

X-ray Diffraction
X-ray Fluorescence
X-ray Micro & Nanotomography



VISUALISATION & SIMULATION

Computed Spectroscopy
Computed Diffraction
Image Simulation & Analysis
Data Mining

CRYSTALLINE MATERIALS

We recognise that seeing and identifying atoms is crucial for researchers working at the nanoscale to solve new scientific problems and create the materials of the future.

New aberration-corrected transmission electron microscopes (TEM) now have electron beams smaller than the spacing between atoms. This means that these TEMs can be used to directly observe atoms and how they are arranged in their crystal lattices.

Microscopy Australia has eight openly accessible, atomic-resolution TEMs with more coming soon. Many have specialised holders that enable researchers to watch and record atomic arrangements change before their eyes as their samples are stretched, squashed, twisted, heated or cooled. Holders can house small areas of gases or liquids, enabling direct observations of electrochemical processes.

SUPPORTING:

MATERIALS SCIENCE

ENGINEERING

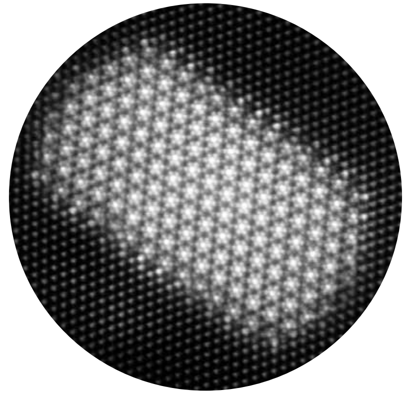
MINERAL EXPLORATION

FUNDAMENTAL PHYSICS

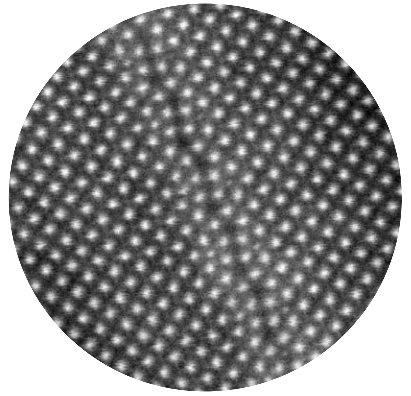
CHEMICAL CATALYSIS

NANOELECTRONICS

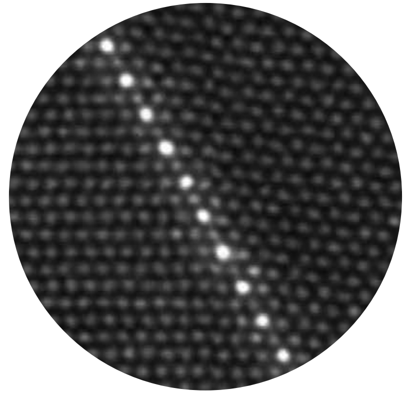
ATOMIC-SCALE TEM OF MATERIALS



Nanoscale cluster of zinc, magnesium and copper in an advanced experimental aluminium alloy – part of a project engineering stronger aluminium alloys at the atomic scale conducted by Li Liu, Keita Nomoto, and Simon Ringer



Atomic-resolution scanning TEM reveals a disruption in the regular arrangement of atoms in a small piece of the mineral tungsten trioxide, from the Zijinshan copper–gold deposit in China. Tungsten trioxide is a well-known semiconductor with applications in materials science, but has not been observed in nature until now. Image captured by Ashley Slattery and Cristiana Ciobanu at the University of Adelaide.



Atomic resolution TEM image reveals the bright gadolinium atoms reinforcing a magnesium alloy. Prof Jianfeng Nie and his colleagues at Monash University have developed this new way to strengthen magnesium alloys to broaden their application.

Reprinted with permission from AAAS.

SEEING ATOMS – REVEALING STRUCTURE

MOLECULES OF LIFE

Understanding the structure of biological molecules is essential to understanding life. An enormous variety of proteins keep us working properly, facilitating chemical reactions and building our tissues. These proteins are intricately folded and extremely structurally complex. They are often organised into multi-molecular complexes and molecular machines. Their structures are directly responsible for their different functions so understanding them is vital to matching structure with function. Preserving proteins with chemical fixatives can destroy this natural structure but snap freezing preserves it most accurately. This is the key feature of cryo-TEM.

Recent technological advances render cryo-TEM capable of elucidating these biological structures at near atomic scale – a huge improvement on earlier instruments. Microscopy Australia is investing in more of these critical instruments to support user demand.

We are also developing our expertise in the emerging technique of microcrystal electron diffraction. This method collects data from tiny crystals too small to be used for X-ray diffraction. It can help determine structures of proteins, organic and inorganic compounds.

SUPPORTING:

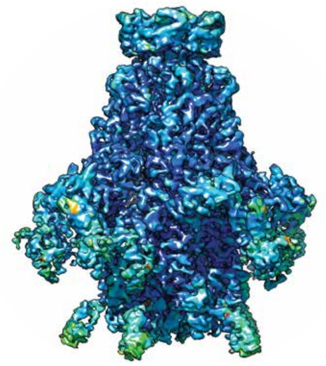
TARGETED DRUG DESIGN

FOOD AND WATER SECURITY

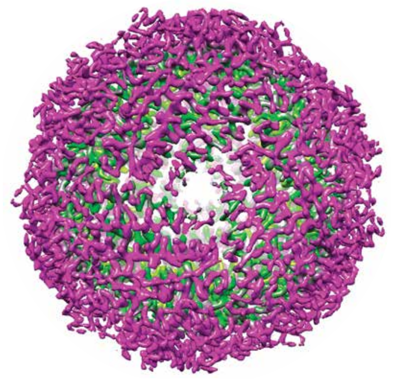
BIOFUEL PRODUCTION

NANOTECHNOLOGY

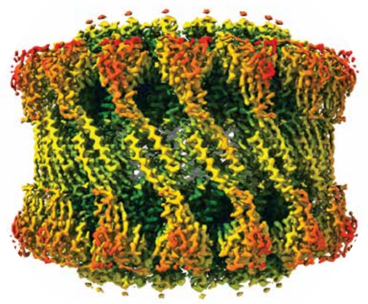
PROTEIN STRUCTURES FROM CRYO-TEM



Structure of a bacterial toxin molecule that has potential applications as an insecticide for use in agriculture, and as the basis for innovative biotechnology and biomedical applications. This structure was determined by using the cryo-TEM at the University of Queensland by Dr Michael Landsberg and his colleagues.



Apo-ferritin is a crucial protein that transports and stores iron in the body. It is a large molecule, which is used by the cryoTEM team at UNSW as a standard to ensure the instrument is performing at its top specification.



The structure of one form of a protein called Perforin-2 that was determined by researchers led by A/Prof. Michelle Dunstone and Prof. James Whisstock at Monash University. This protein helps the immune system to get rid of invading microbes by making holes in their membranes.

IMPACT PATHWAY

Microscopy Australia is a critical piece in the research infrastructure that keeps Australia at the forefront of global innovation. See how we impact Australia and the world.

INPUT

- Microscopy and microanalysis experts
- Instruments, tools and techniques
- Commonwealth NCRIS funding
- Institutional funding
- State government funding

ACTION

- Forecasting and procurement of emerging technologies
- Comprehensive training for beginners to experts
- Providing industry and researchers with access to instruments, techniques and experts
- Stakeholder engagement, meetings and workshops
- International collaborations and staff exchange
- Access programs for start-ups, SMEs and spinoffs

OUTPUT

- Scientific breakthroughs and discoveries
- Industry innovation
- Development of new techniques and tools
- Improved methods and best practice
- Cost-savings through national coordination of instrument purchases
- Highly trained users and students

OUTCOME

- World leading research
- New companies - start ups and SMEs
- New products and patents
- Innovation delivery
- Adoption of our new techniques and tools by the international community
- Consolidation of Australia's research reputation

OUR IMPACT

REAL WORLD OUTCOMES

SOCIETY

Microscopy Australia is enabling new treatments and solutions for health and wellbeing

FIGHTING DISEASE

Cryo-TEM is helping to find new approaches to beating antibiotic resistance.

FOOD SECURITY

Research into Biochar – using garbage to improve agricultural yields and reduce carbon dioxide emissions.

VACCINATING THE WORLD

Microscopy Australia supported the development of the Nanopatch which will help to eradicate infectious diseases by making vaccination programs more effective worldwide.

ECONOMY

Microscopy Australia is enabling innovation to build business and prosperity

REGIONAL DEVELOPMENT

Outback spinifex is building business as its nanofibres strengthen condoms and surgical gloves.

REINFORCING THE FUTURE

Graphene Manufacturing Group uses electron microscopy to tailor their products to meet their clients' needs.

MINERAL EXPLORATION

Geological Survey WA and Minerals Research Institute of WA use ion probes at our University of Western Australia facility to understand how ore bodies form for more effective mineral exploration.

ENVIRONMENT

Microscopy Australia is enabling more sustainable solutions for our future

RENEWABLE ENERGY

Nanotechnology for the integration of solar cells into buildings and solar farms benefits both economy and environment.

ENVIRONMENTAL REMEDIATION

New polymers made from waste can absorb mercury and oil spills for a cleaner environment.

ENGINEERING SUSTAINABILITY

Alloys engineered at the atomic scale to be lighter and stronger, will reduce the environmental impact of transport and construction.

ENABLING BUSINESSES TO PROSPER

linear

Linear is accessing our flow cytometry to attract and conduct international clinical trials.

GMG Graphene Manufacturing Group

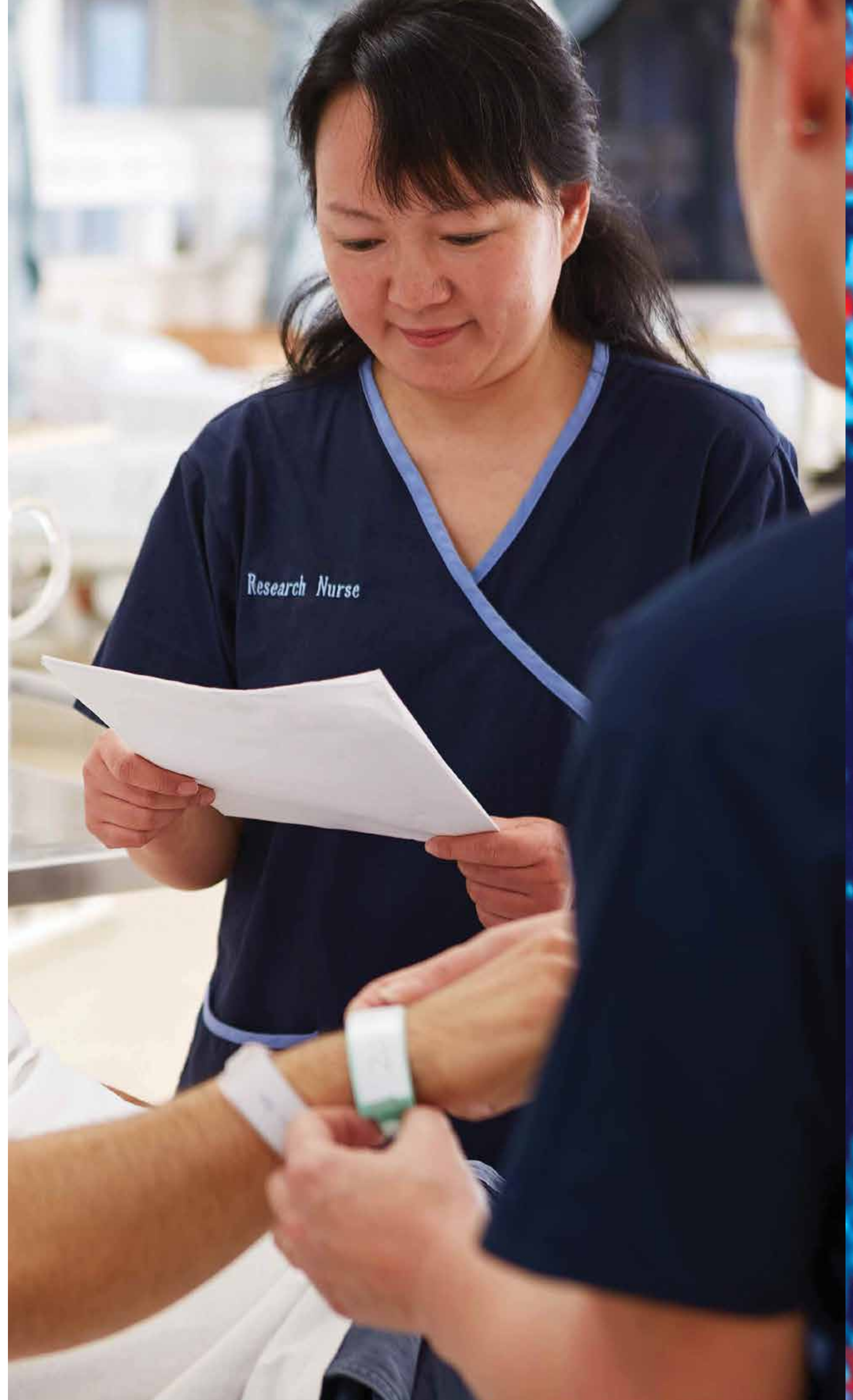
Graphene Manufacturing Group – accessing microscopy for fast turnaround production management.

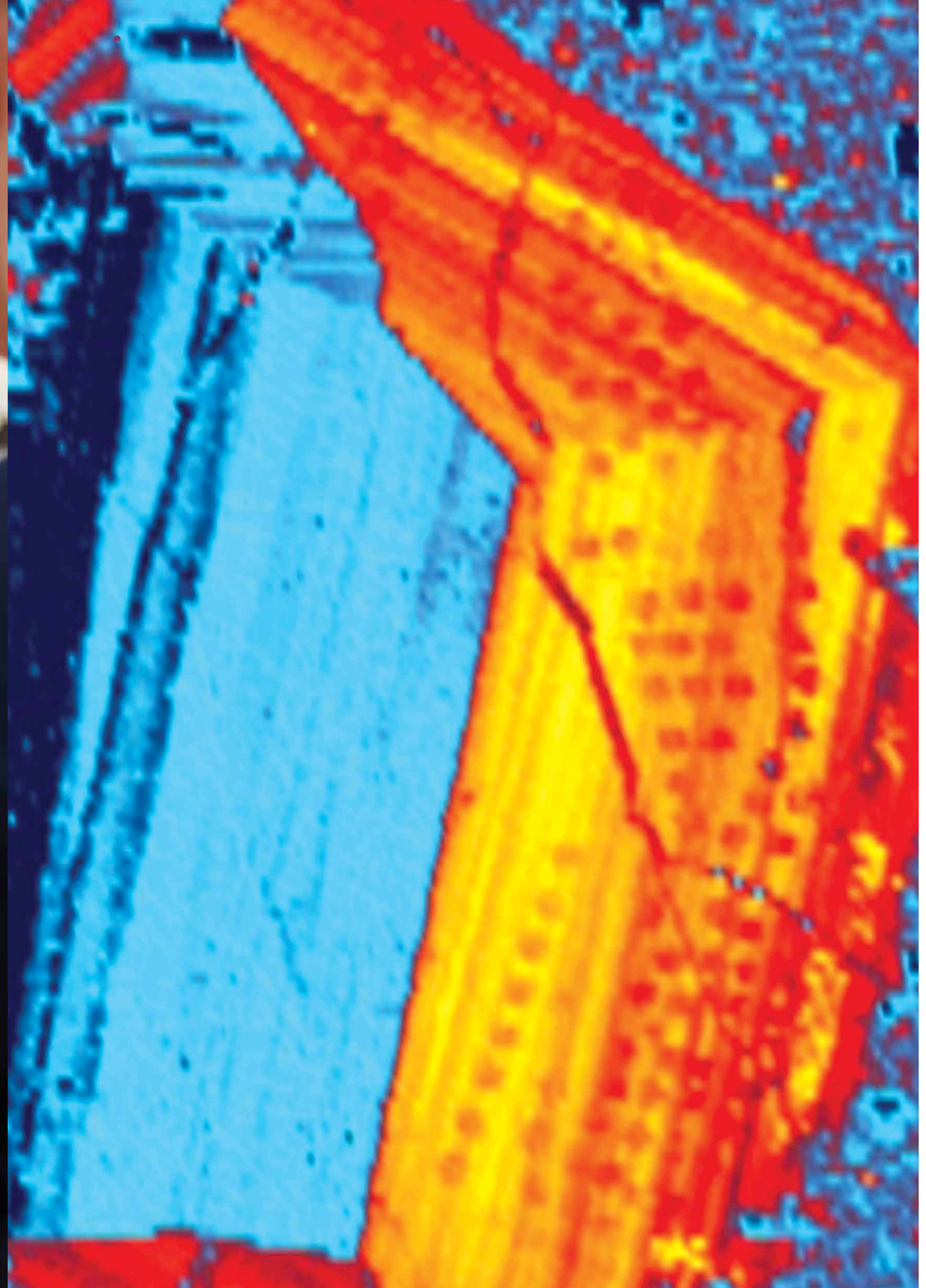
WearOptimo

Wear Optimo is benefiting from complimentary microscopy techniques at different facilities to support their R&D.

membraneworks

Membrane Works use our SEMs to enable their business analysing water treatment filters.





BHP

BHP is a household name in global resources. It directly employs approximately 4500 people in South Australia where it operates the Olympic Dam mine. This is one of the world's largest ore deposits where copper, uranium, gold and silver are mined and processed in a fully integrated and unique processing facility.

For cost-effective exploration BHP needs to understand how the Olympic Dam ore body formed. Microscopy is essential for this, enabling them to examine and understand the structure of minerals at the nanoscale across the entire deposit. To maximise efficiency, they must also understand how each mineral responds in the complex processing facility.

Trouble-shooting any performance issues with the metallurgical plant requires immediate microanalytical analyses of minerals. Although BHP do not own and operate micro-analytical facilities they use the Microscopy Australia facilities at the University of Adelaide and have done since 1992.

BHP is also involved in a significant number of ARC co-funded geology and metallurgy projects, and analytical infrastructure proposals. Microscopy Australia facilities at the University of Adelaide, University of Western Australia and Curtin University, along with other facilities at the University of Tasmania and the University of Melbourne are used to support these research activities.

“I would like to stress the importance of Microscopy Australia facilities, including the highly skilled, professional staff who operate the facilities, to the mining industry within Australia. Some of the industry, like BHP Olympic Dam, directly use your facilities, whereas other parts of the industry use the facilities indirectly by supporting university-based research projects. The quality of ore being mined throughout the industry is gradually declining and it is becoming more challenging to extract the metals in a cost-effective way. We therefore need to tailor our processing facilities to cater for the minerals present in the ore. This is only achieved by characterising our minerals down to the nanoscale.

Kathy Ehrig, Superintendent Geometallurgy – Olympic Dam BHP.”

ENGAGING WITH THE WORLD

INTERNATIONAL STAFF SHADOWING

As part of the Microscopy Australia Staff Shadowing Program, Jacob Byrnes from the University of Sydney visited the TEM Station at the National Institute of Materials Science (NIMS) in Japan, focusing on advanced specimen preparation techniques for materials.

"

The lab visit allowed me to gain perspectives on how a lab similar to my own could be managed. Learning how equipment training is managed and how the lab is organised was particularly valuable and inspiring. The visit also gave me great insights into their approach to training and the expectations they have for their users."

"The breadth of content and the exceptional quality of their manuals and guides has inspired me to introduce similar resources to my own lab, which I believe will improve the overall efficiency of training. Other fantastic organisational ideas have led me to reorganise the layout of my own lab. I also learnt valuable specimen preparation tips and tricks that will ultimately benefit the user-base of Microscopy Australia.

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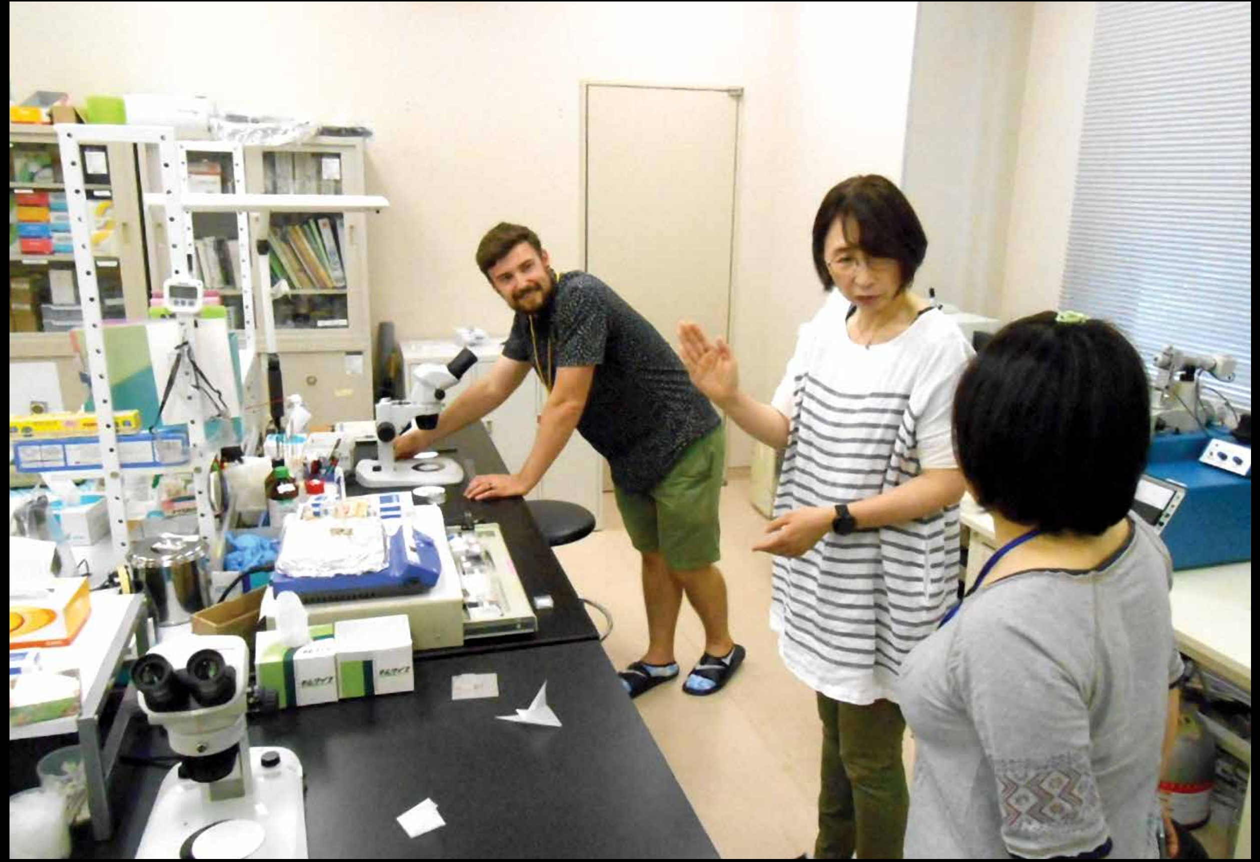
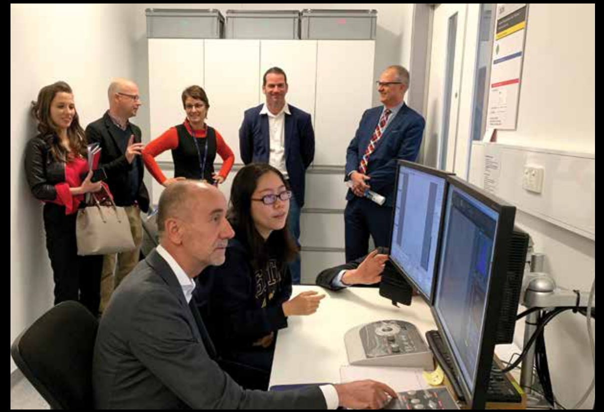


EU COMMISSIONER VISITS MICROSCOPY AUSTRALIA

Jean Eric Paquet – Director General – Directorate Research and Innovation, European Commission and his delegation visited Microscopy Australia's University of Sydney facility to discover the nature and management of our national microscopy research infrastructure.



STRATEGIC CONNECTIONS FOR GLOBAL IMPACT

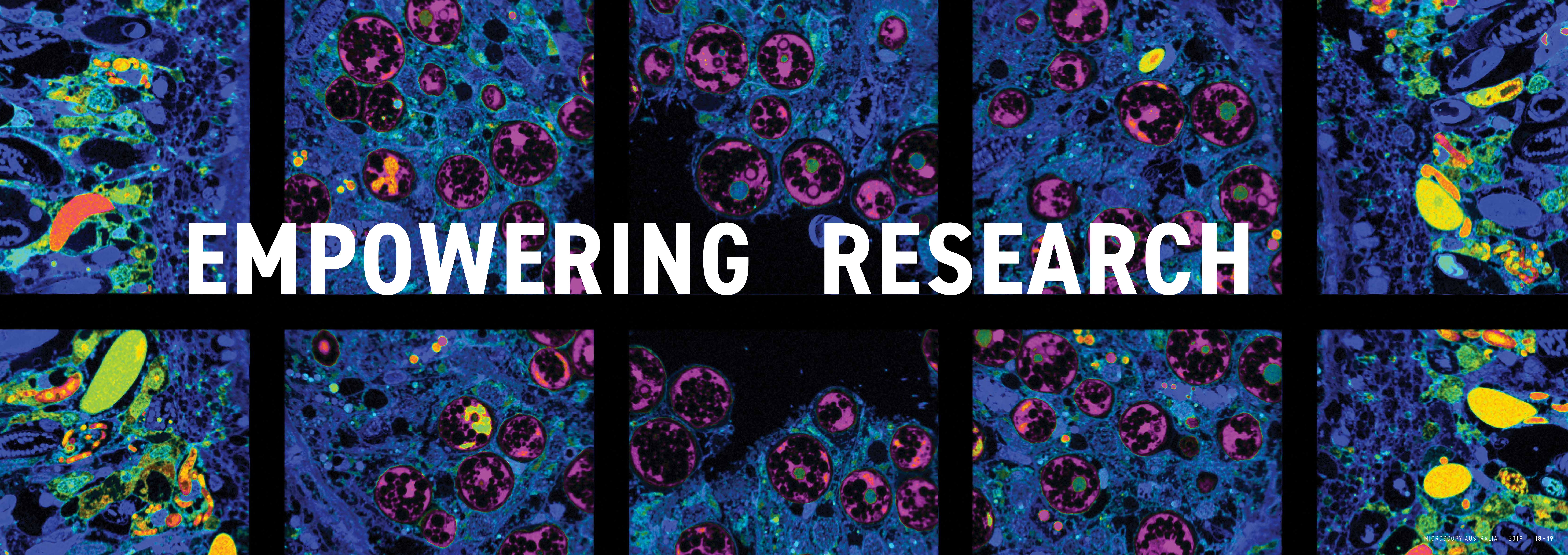
Microscopy Australia works with Australian and international organisations, forming strategic links to enhance access to microscopy and microanalysis facilities and to share our expertise in implementing collaborative national research infrastructure.

Microscopy Australia is part of Global BioImaging, which hosts an international Exchange of Experience (EoE) Workshop series. The most recent, EoE IV, was hosted by SingaScope – a Singapore-wide microscopy infrastructure network. It brought together partners and delegates from across the growing Global BioImaging network, including representatives from Australia, Canada, Europe, Japan, Mexico, Singapore, South Africa and the USA. The program focussed on career paths for core facility staff and the future activities of the Global BioImaging network. Microscopy Australia representatives attended the workshop, along with colleagues from the National Imaging Facility. Microscopy Australia delegates participated in various Working Groups on Career Paths, Image Data Management, Social Impact and Quality Management in Research Infrastructure. Similar challenges in these areas are being encountered across the global research infrastructure community. A series of discussion papers from the Working Groups are now being developed.

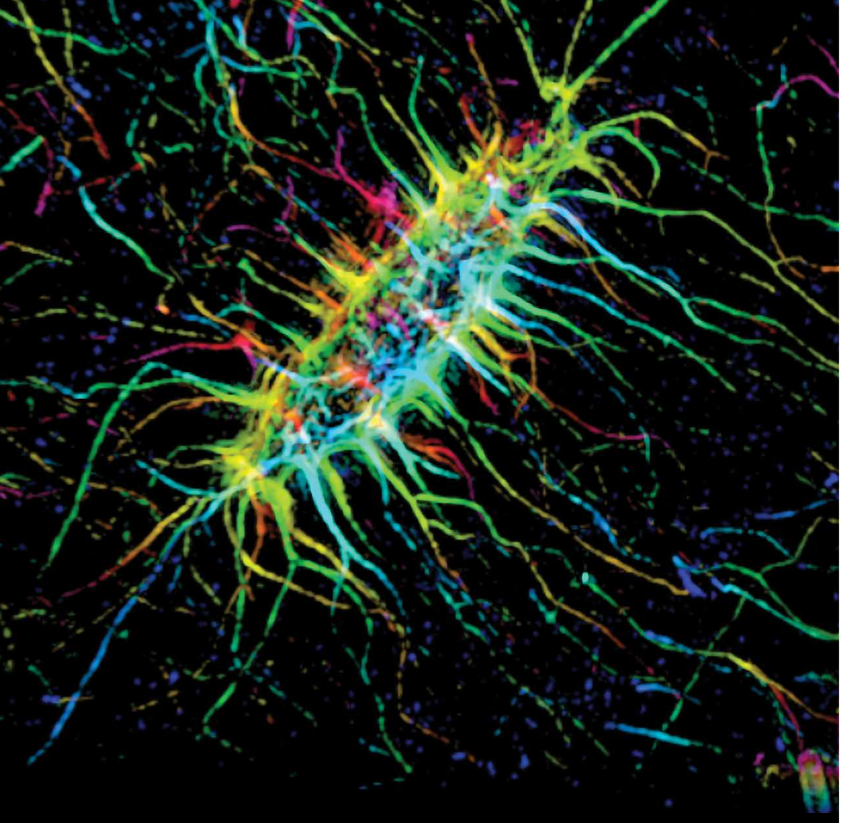
During the Exchange of Experience Workshop, the collaboration framework between Microscopy Australia and Euro-BioImaging was signed, continuing the partnership until September 2021.

AFRICAN OPPORTUNITIES BECKON

A Nigerian delegation, including the Nigerian Ambassador to Australia, visited the Microscopy Australia facility at the University of Western Australia as part of a study tour to support Nigeria's increasing investment in minerals and mining. Their aim was to open opportunities for possible collaboration and mentorship with suitable Australian facilities in the areas of technical capacity building and enhancement of their processes.



EMPOWERING RESEARCH



MyScope

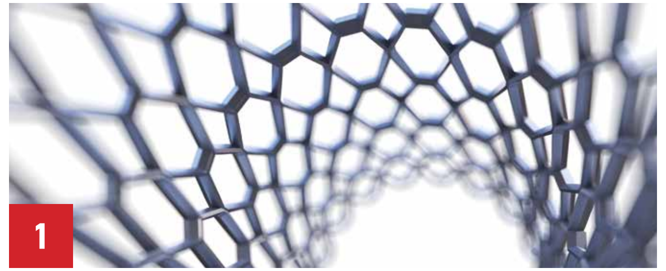
Explore our online platforms to train in advanced microscopy:

myscope.training

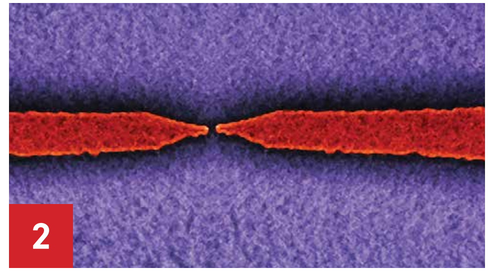
Introduce your family to microscopy with our engaging simulator activities:

myscope-explore.org

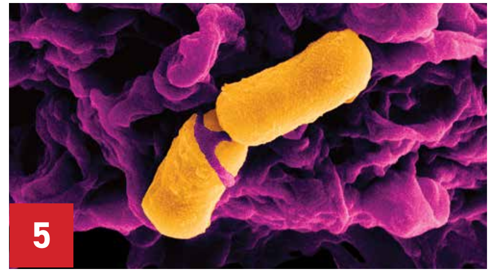
Image: Confocal image of a bone cell, colour coded to show the height above the surface. Dr Junjie Gao, Perron Institute, UWA.



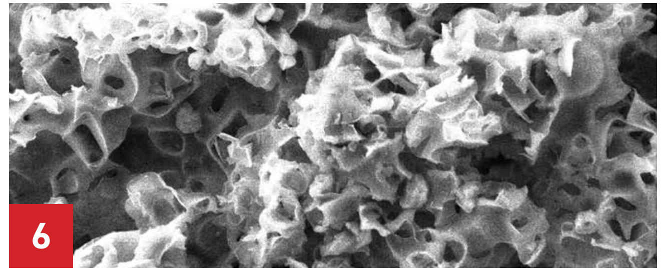
NANO-LANDSCAPE CONTROLS INFLAMMATION



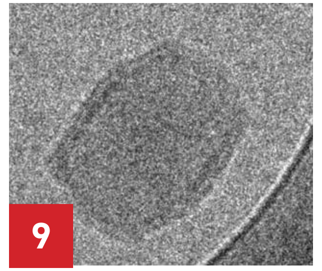
TRANSISTORS FROM THIN AIR



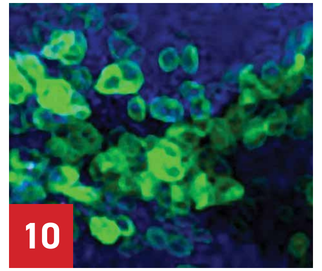
BEATING B. CEREUS



SUSTAINABLE NEW POLYMERS FROM WASTE



SHAPE SHIFTING AT THE NANOSCALE

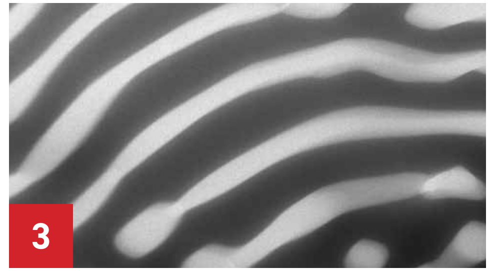


ORIGINS OF CHRONIC PAIN

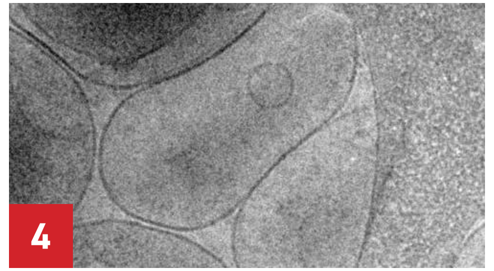
NUTRIENT MANAGEMENT – KEY TO SURVIVAL

RESEARCH OUTCOMES & SOCIAL IMPACT

Take a closer look at this year's research highlights – all enabled by Microscopy Australia. With over 3,900 researchers annually, here are just a few of our recent stories.

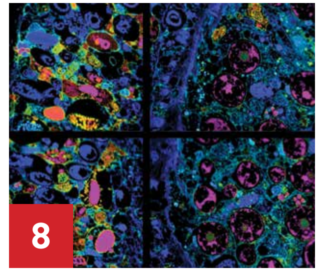


DESIGNING ALLOYS FOR A HIGH PERFORMANCE FUTURE

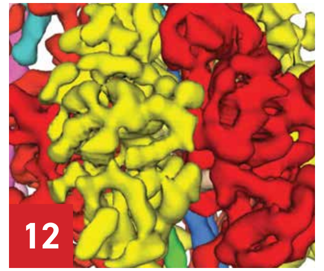


COORDINATING RESPONSE TO EXERCISE

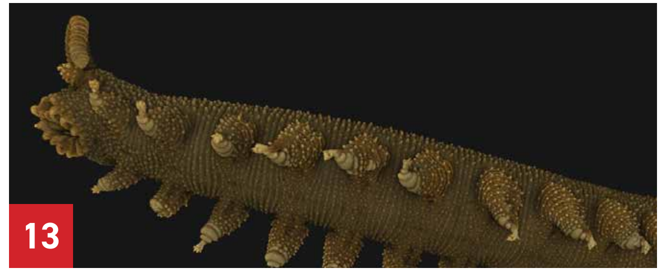
CLEANING THE SYDNEY HARBOUR BRIDGE



ZOOMING IN ON BIG PROBLEMS

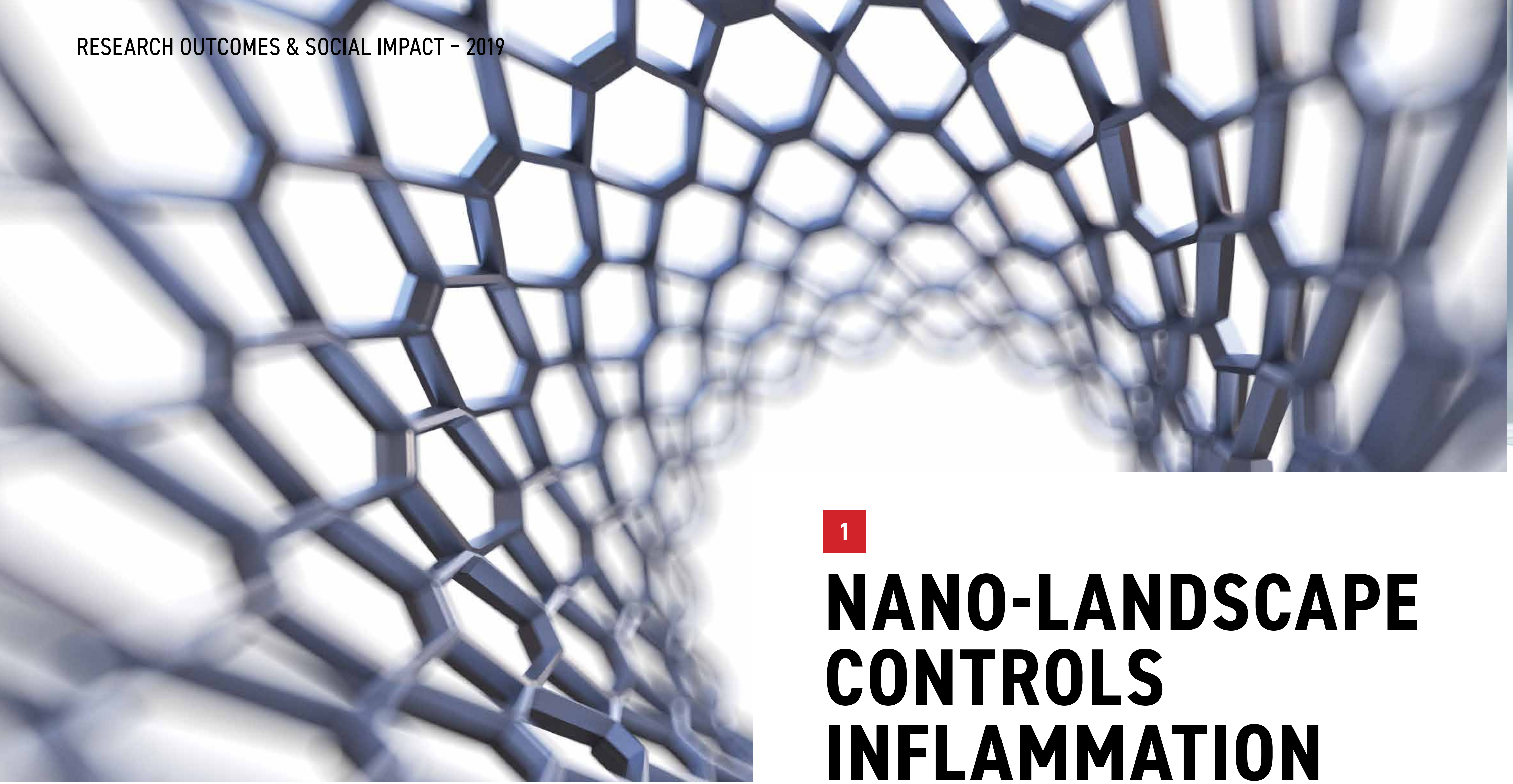


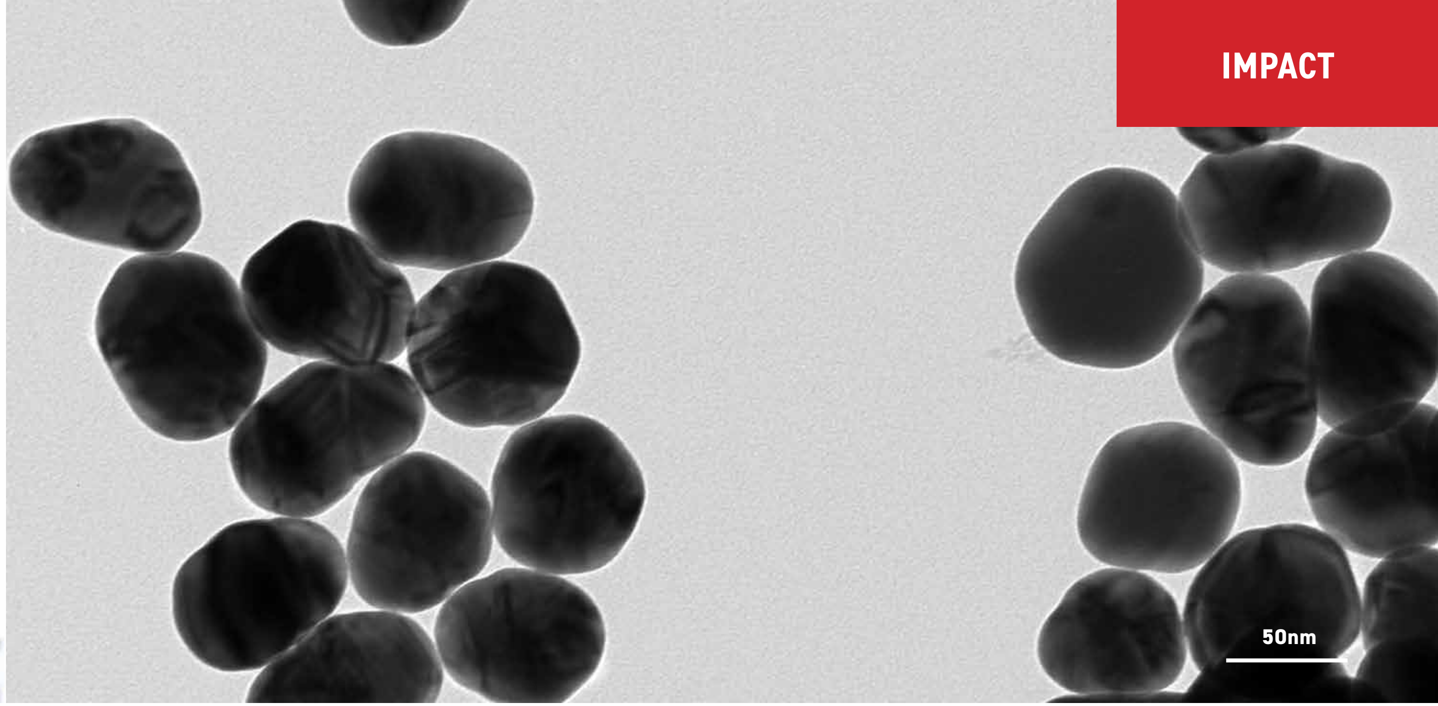
BEATING THE BACTERIA



MUSEUMS LOOK TO THE FUTURE

2019





1

NANO-LANDSCAPE CONTROLS INFLAMMATION

Findings reveal a link between surface features, protein unfolding, and immune responses.

CHALLENGE

Medical devices are central to modern regenerative medicine to enhance, replace and restore organs or bodily functions. However, their performance is often compromised by bad reactions from the patient's immune system in response to the foreign materials. Nanoscale structures on the surface are known to affect how the body responds but we don't know much about how they do this. This makes it difficult to design devices with predictable interactions with cells.

RESEARCH

Researchers at the University of South Australia (UniSA) led by Prof. Krasimir Vasilev have recently published the first evidence that the scale of surface features affects the shape of a large protein called fibrinogen. This protein mediates inflammatory responses, blood clotting and other blood processes. Researchers at the University of Queensland had found that free-floating nanoparticles of different sizes can make fibrinogen unfold and stimulate immune responses. Prof. Vasilev thought this could also be the case for nanostructured surfaces. His research team attached 16, 38, and 68 nanometre diameter gold nanoparticles to surfaces at different densities to see what effect this had on fibrinogen and the immune system.

The team used a multitude of microscopy and microanalysis techniques at the Microscopy Australia facility at UniSA, combined with an array of other analytical techniques. They found that surfaces with 16 and 68 nanometre features increased inflammation whereas the opposite was seen for 38 nanometre nanofeatures, where inflammation was reduced. This is likely to be related to the fact that fibrinogen is 45 nanometres long and would be less strained when it interacts with the 38 nm particles. The smaller and larger particles cause fibrinogen to bend more and expose internal parts of the molecule that are not normally seen be the immune system.

These findings reveal the link between surface features, protein unfolding, and immune responses. They also show that by carefully tailoring surface nanotopography, biomedical engineers will be able to effectively control the inflammatory response induced by implanted materials.

IMPACT

- Safer biomedical devices
- Improved patient satisfaction and quality of life
- Reduced health burden associated with implants
- Reduced economic burden due to adverse reactions from implanted devices

Ref. R.M. Visalakshan et al. 2019, Adv. Funct. Mater., 29, 1807453

Image above: TEM image of 68nm nanoparticles

2 TRANSISTORS FROM THIN AIR

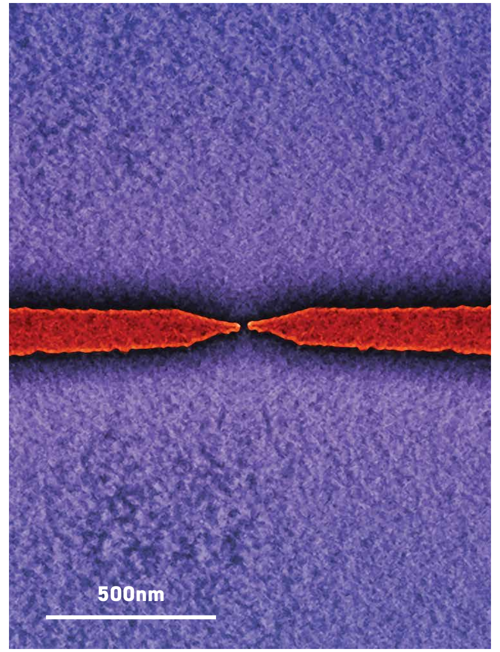
The transistor is the building block for all electronics, and typically involves sending electrical currents through silicon. Every computer and phone has millions to billions of silicon electronic transistors, but this technology is reaching its physical limits where the silicon atoms get in the way of the current flow, limiting speed and causing heat.

Ms Shruti Nirantar, A/Prof. Sharath Sriram and their team of researchers at RMIT University, have engineered a new type of transistor that sends electrons through nanoscale air gaps without the need for any semiconductor. At the nanoscale the number of air molecules in the gaps is insignificant. Therefore, no collisions occur to slow down electron flow and to produce heat.

Ms Nirantar has tested electrodes made of tungsten, gold and platinum for their electron emission properties. She found that the performance depends on the material properties of the metals, especially for stability and the on/off ratio. Their finding proves tungsten-based transistors to be ideal for practical applications, although the properties of the different metals could bring benefits in different scenarios.

The team has used the Australian National Fabrication Facility to make their test devices and the Microscopy Australia Linked Laboratory at RMIT to study the device structure and identify operation mechanisms. Microscopy showed that the gaps between electrodes were small enough (11–34nm) for electrons not to encounter significant interactions with air molecules.

Research leader A/Prof. Sriram said that the design solved a major flaw in traditional solid channel transistors. This promising proof-of-concept design for nanochips could revolutionise electronics although a great deal of further work is required to make such devices a reality.

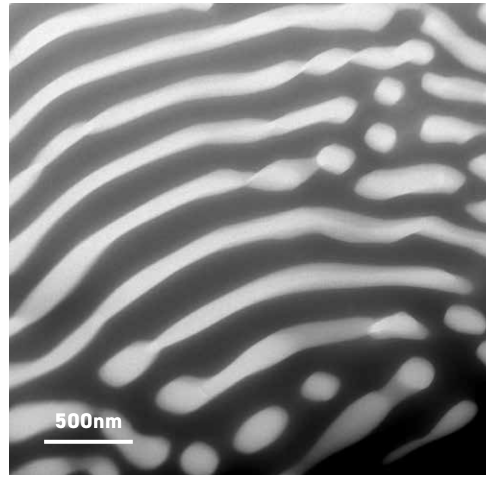


Colour-enhanced SEM image of a nanoscale gap in a metal electrode pair with strong electron transport.

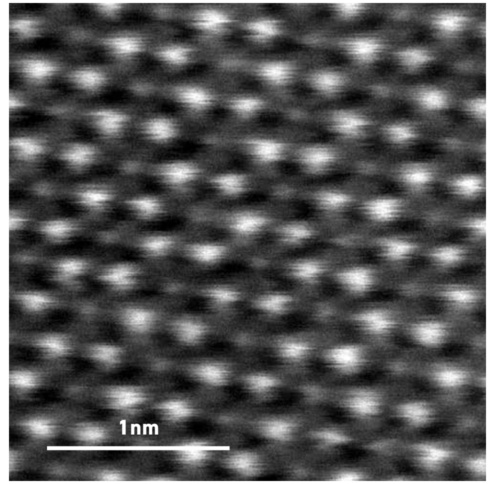
3 DESIGNING ALLOYS FOR A HIGH PERFORMANCE FUTURE

Alloying of metals can bring improved properties such as strength or malleability to make new materials that are better suited to various structural applications. However, strength and malleability are almost mutually exclusive so finding innovative ways to bring them together is a challenge being addressed by many researchers. One of these is Dr Yujie Chen at the University of Adelaide (UA). She has developed a micro-structured multi-metal alloy, designed with two phases (the dark and light bands in the image); the dark phase provides good malleability while the white phase gives the material high strength.

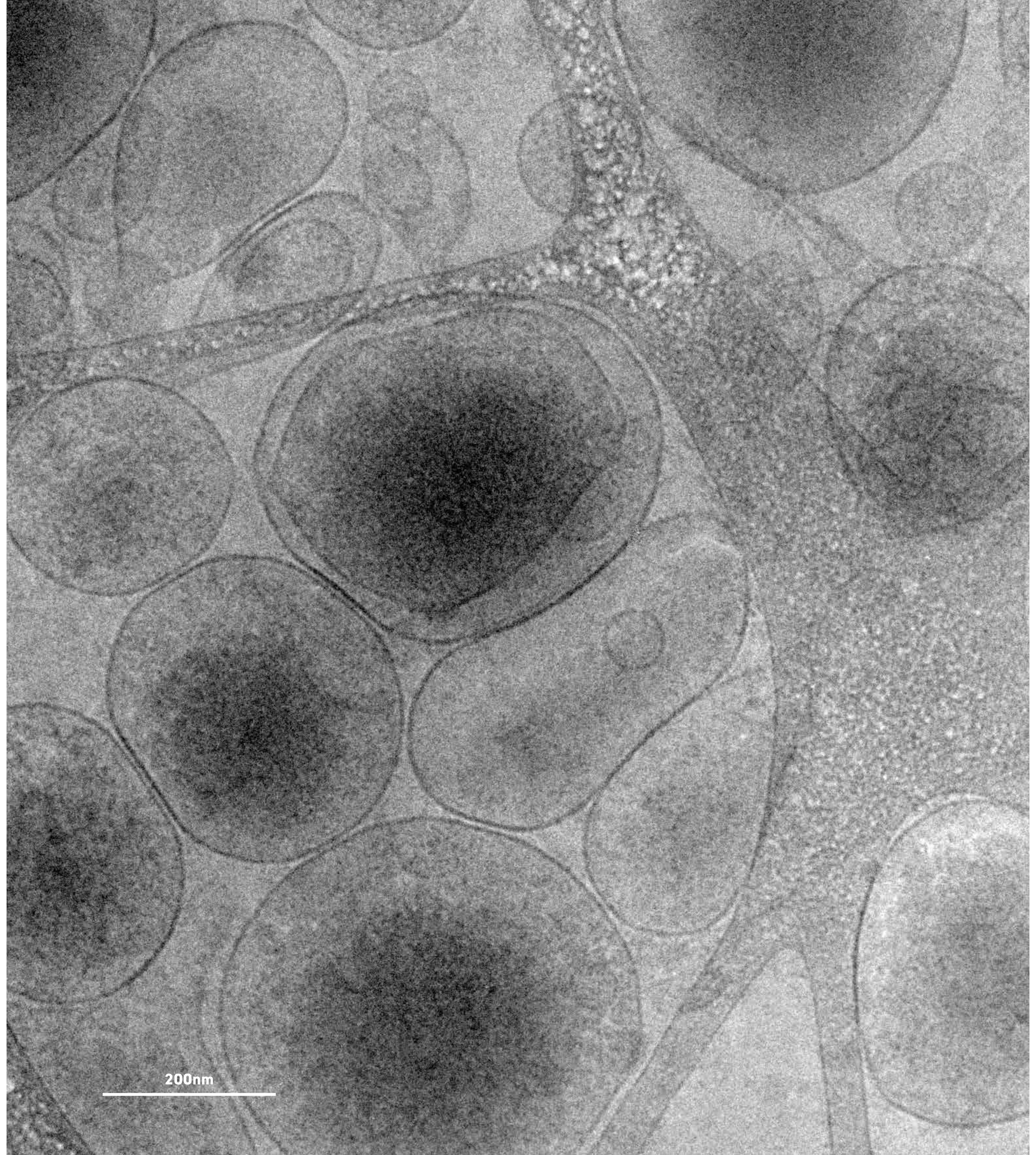
This combination of properties results in an alloy with extremely high performance, and tuneable properties depending on the microstructure and the materials chosen for the phases. High resolution scanning transmission electron microscopy (STEM) conducted in the Microscopy Australia facility at UA revealed the crystal structure of the stronger (lighter colour in the striped image) phase. It shows that the atoms of two metallic elements are arranged in a hexagonal structure, while the more malleable (darker) phase has another set of metal elements arranged in a face-centred-cubic (FCC) microstructure. Understanding the structure in this way enables the research team to make alterations to incorporate specific properties into their alloys to address particular functional needs.



TEM image showing the two phases in the alloy



High resolution STEM image of the hexagonal arrangement of atoms in the lighter phase. The atoms show up as lighter dots against a black background.



4 COORDINATING RESPONSE TO EXERCISE

Exercise is important for a healthy body and mind and gives rise to a complex set of biochemical changes in many different tissues. These are largely due to the increased metabolic demands of contracting skeletal muscles. Since some tissues are clearly working much harder than others the changes need to be coordinated to keep the body functioning within the normal range and, in the longer term, produce the physical adaptations associated with improved health and wellbeing.

A lot of different molecules have previously been identified that are secreted directly into the blood. They travel around the body and stick onto matching receptors in various tissues where they have their effects. It is also known that some signalling proteins travel around in the blood encapsulated in fatty coats. These packages are called extracellular vesicles (EVs).

A large international research team led by Mark Febbraio at the Garvan Institute, combined proteomics and microscopy in the Microscopy Australia facility at UNSW, to study changes in the protein profile during exercise. 300 exercise-specific proteins were detected, including 35 newly described proteins released by muscles and transported in EVs. They also found that EVs liberated by exercise tend to localise to the liver where they deliver their protein cargo. This is not surprising as the liver has a whole range of important roles in regulating our metabolic processes.

The discoveries made from this research identified a new paradigm by which tissue crosstalk during exercise can exert biological effects throughout the body.

Image: TEM image of extracellular vesicles

FOODBORNE DISEASES AFFECT AROUND 600 MILLION PEOPLE EACH YEAR WITH HUNDREDS OF THOUSANDS OF DEATHS

Image: Colour-enhanced scanning electron micrograph showing a battle between a macrophage (magenta) and two rod-shaped B. cereus (orange).

5

BEATING BACILLUS CEREUS

CHALLENGE

Foodborne diseases are a major health burden worldwide, affecting around 600 million people each year with hundreds of thousands of deaths. Foodborne bacteria and their toxins can cause diarrhoea and vomiting by damaging the intestinal lining and triggering inflammation. If the bacteria break through the intestinal lining into the bloodstream, they can cause septic shock and death. Antibiotic resistance is a serious problem that prevents effective treatment of these dangerous bacteria. More knowledge on how the immune system fights these disease-causing bacteria will help us to develop alternative treatments.

RESEARCH

Prof. Si Ming Man and his team at the Australian National University (ANU) have identified a toxin called HBL, produced by the widespread foodborne bacteria, *Bacillus cereus*. These bacteria attack the intestinal lining causing diarrhoea and vomiting but if the bacteria get through into the blood stream the resulting septic shock can be fatal.

Immune cells called macrophages are the key to the lethality. These macrophages exist in tissues, including the intestine, and the blood (where they are called monocytes). When the toxin enters the macrophages, as well as forming holes in the membrane, which will lead to the cell's death, it triggers a sensor that alerts the rest of the immune system to come and attack the bacteria. As long as the bacteria stay contained in the intestine, this gut-based immune response will eventually overwhelm the bacteria and the person recovers. However, if the bacteria reach the blood, the HBL toxin they release will attack other cells around the body, including many more macrophages/monocytes. This reaction causes massive inflammation all over the body, which can cause septic shock and death. This is when the inflammation needs to be stopped.

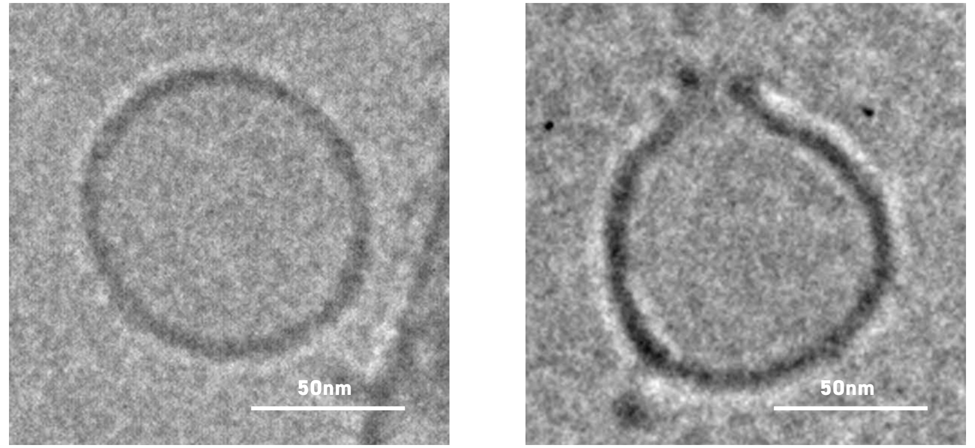
Scanning electron microscopy in the Microscopy Australia facility at ANU revealed to the researchers how the bacteria stick to the macrophages and transmission electron microscopy showed that the HBL toxin causes holes in cell membranes.

By connecting the action of the *B. cereus* HBL toxin with the sensor inside the macrophages, the researchers have identified that a molecule called MCC950 blocks the sensor and completely prevents death from *B. cereus* infection in mice.

IMPACT

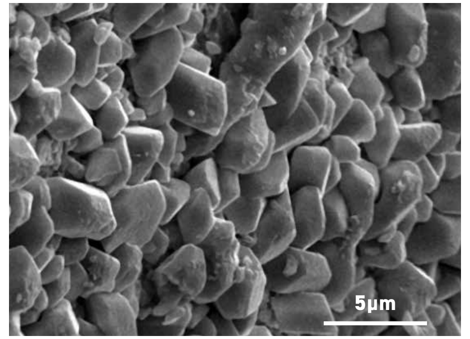
- Potential effective treatment of *B. cereus* infections in humans
- New and universal strategy to tackle infection with toxin-producing bacteria
- Millions of lives saved
- Reduced economic burden

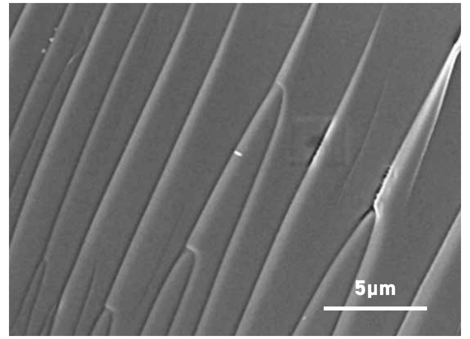
Refs: Mathur, A, et al. (2019) Nature Microbiology. 4: 362–374.



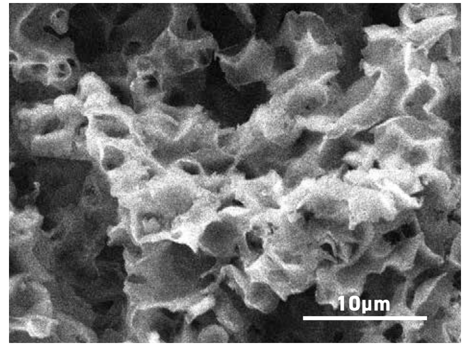
Cryo-transmission electron micrograph showing an untreated liposome (left) with intact membrane and a toxin-treated liposome with a membrane pore (right).

Dr Max Worthington and A/Prof. Justin Chalker in the lab with samples of their polymers





SEM images of cut surfaces of polymers without salt templating. Top, sulfur crystals form on the cut surface of the polymer made with lower levels of DCPD but not when the DCPD level used is higher – bottom.



Polymer deposited around nanoscale salt crystals, which are then removed. This creates a porous 'sponge' with high absorbancy.

6

SUSTAINABLE NEW POLYMERS FROM WASTE

CHALLENGE

Modern plastics, rubbers and ceramics are ubiquitous in our everyday lives. Unfortunately, many of these materials cannot be recycled and often accumulate in waste streams and the environment.

There is a need for next-generation recyclable plastic, rubber, and ceramics designed with controllable properties, such as hardness, flexibility, colour, and transparency.

RESEARCH

We have previously covered A/Prof. Justin Chalker's (from Flinders University) work on polymers for environmental remediation and here he is extending that work into new application areas. He has co-led a team in a collaboration with Dr Tom Hasell at the University of Liverpool, providing precise new design principles for controlling the properties of plastic, rubber, and glass made from sulfur – an abundant waste product of the petrochemical industry. For instance, making a polymer from sulfur, canola oil and dicyclopentadiene (DCPD) provides several different types of materials. Add more canola oil, it is a soft rubber; add more of the rigid dicyclopentadiene and the material becomes harder and more durable.

Reacting sulfur, limonene (waste product of the citrus industry) and dicyclopentadiene at various ratios can provide materials from soft waxes to hard glass.

In yet another example, terpinolene (an essential oil found in allspice and other plant products) was reacted with sulfur to form an orange transparent film. By adding in dicyclopentadiene during the reaction, the colour could be tuned from orange to red to black (image below). The dicyclopentadiene also made the film retain its shape better at higher temperatures.

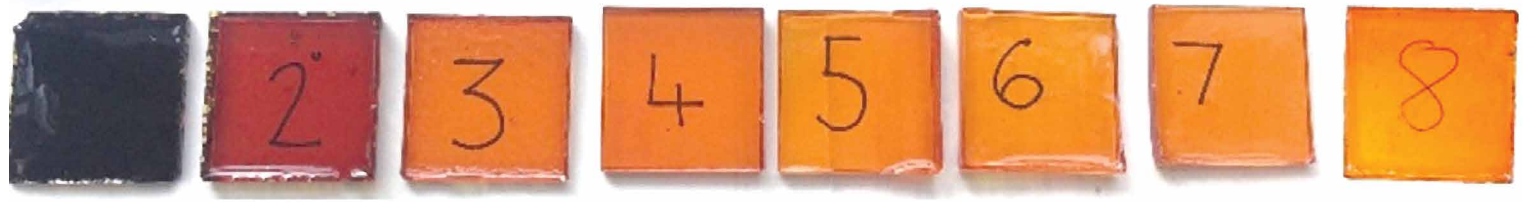
Sulfur has very different properties to carbon, and this may lead to many interesting new applications for these polymers.

IMPACT

As most polymers are made directly from our limited reservoir of petrochemicals, every kilogram of sulfur (we generate 100M tons each year) we use to make polymers, saves petrochemical resources and reduces its waste.

As well as environmental remediation, sulfur polymers have potential in:

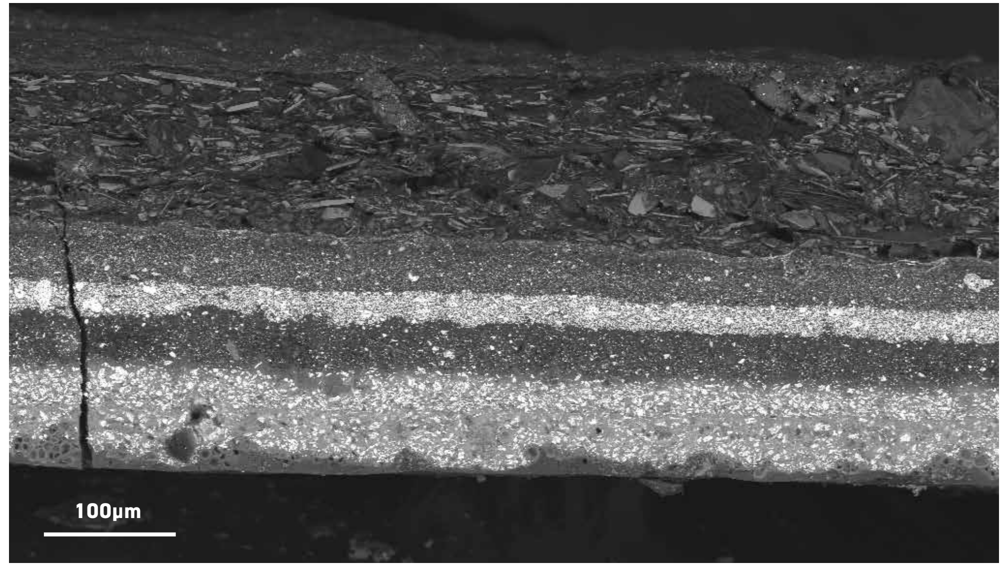
- construction, especially where thermal insulation, electrical insulation, and chemical resistance are important
- high capacity batteries that are more stable to repeated charge/discharge cycles
- lenses and optical filters in IR thermal imaging, night-vision lenses, and LIDAR
- agriculture.

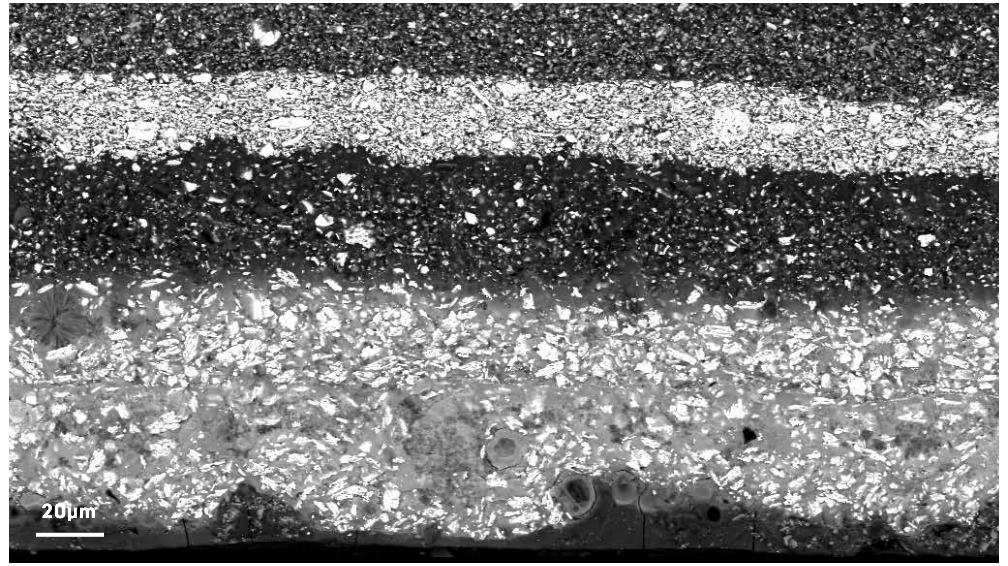


50% DCPD	35% DCPD	30% DCPD	25% DCPD	20% DCPD	15% DCPD	10% DCPD	0% DCPD

7

CLEANING THE SYDNEY HARBOUR BRIDGE





CHALLENGE

The Sydney Harbour Bridge was opened in 1932 and not surprisingly, is a heritage-listed structure. A mammoth effort is required to look after the Bridge to keep it looking its iconic best. Cleaning the paint and stone, and replacement of aging and damaged paint is a major part of this.

Dirt, rust and the existing lead-based paint are currently removed by sand blasting. New lead-free paint is then applied. However, the Bridge arches hide 7.2 km of tightly confined tunnels where sand blasting is essentially impossible. Restricted operating space and the removal of the waste material are serious challenges. Laser cleaning, which generates largely airborne filterable waste is an alternative approach to resolving this problem.

RESEARCH

A collaborative ARC Linkage Project has recently got underway at the Australian National University (ANU) on laser cleaning processes for the Sydney Harbour Bridge. It aims to refine new laser-based approaches to large scale paint stripping and processing of corroded metal and dirt-encrusted stone surfaces. Older laser methods generate extreme heat on the surfaces being cleaned, which can melt the surface of steel. In contrast, the new techniques use ultrashort laser pulses in the femtosecond (a million times shorter than a nanosecond) range. This is so fast, that the paint instantly evaporates, leaving the underlying metal structure intact and cold. Paint can therefore be removed without heating or altering the underlying structure.

The researchers, Prof. Andrei Rode and A/Prof. Stephen Madden, used scanning electron microscopy (SEM) at the ANU facility of Microscopy Australia, to study the effect of the laser treatment on the underlying steel and modify their process accordingly.

Their method accomplished cleaning without heat-damage and with reduced energy consumption whilst being economically and time competitive with established industrial-scale cleaning technologies such as sand blasting. The realisation of the new process drew extensively on world-leading fundamental physics explorations of ultrafast laser ablation carried out at the ANU over the last 15 years.

The project is a collaborative venture with ANSTO, the University of Sydney, the University of Canberra and Transport for New South Wales (Project LP180100276).

IMPACT

- The potential to maintain the integrity of the Bridge and save millions of dollars in infrastructure maintenance
- A fully optimised process that could transform the future of global infrastructure maintenance
- Applications in conservation projects as well as the aerospace, automotive and marine industries

Images: SEM images of cross sections of paint flakes from the Sydney Harbour Bridge showing past layers of paint.

8 ZOOMING IN ON BIG PROBLEMS

In the wake of a changing climate, it is imperative to understand how significant ecosystems, especially marine systems, will be impacted and how changes are mediated. Dr Jean-Baptiste Raina at the University of Technology Sydney's Climate Change Cluster (C3) is investigating these changes in collaboration with Microscopy Australia's NanoSIMS facility at the University of Western Australia (UWA).

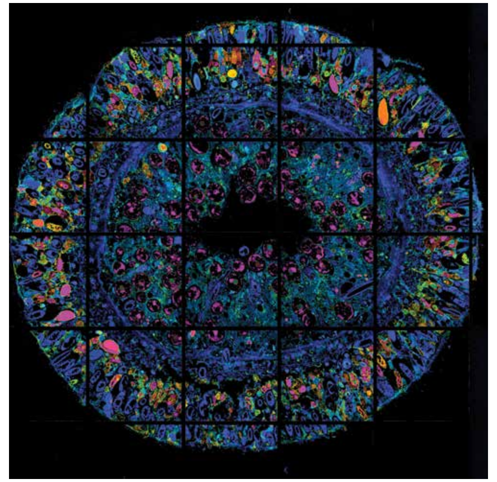
The nanoSIMS makes possible the precise micro-scale investigations necessary to study the microbes that drive most of the important processes involved in ocean health. Dr Raina uses the nanoSIMS to understand how microbial inhabitants of larger marine organisms, such as corals and anemones, contribute to ecosystem health and how isolated microbes process nutrients in a changing environment. His research has also contributed to understanding natural climate regulation by identifying how dimethyl sulfide (DMS) and its precursor, dimethylsulfoniopropionate (DMSP) are produced in algae. These globally important molecules are important info-chemicals, key nutrients for marine microorganisms, and are involved in global sulfur cycling, atmospheric chemistry, cloud formation and associated cooling effects.

Dr Raina found that both corals and their symbiotic algae have the 'machinery' to produce DMSP. This highlights the double jeopardy of worldwide declining coral cover: less coral means less DMSP is made, resulting in less cloud cover and contributing to more warming.

The research team is now combining nanoSIMS analyses with sophisticated genetics-based approaches to investigate how different coral and symbiont variants can tolerate changing environmental conditions. He has generated seven publications in collaboration with the UWA nanoSIMS facility with other projects ongoing and future projects anticipated.

Ref. Andrew R. J. Curson et al., 2018, Nature Microbiology (3), pp430–439

Nils Rädecker et al., 2018, Front. Physiol., 16 March, https://doi.org/10.3389/fphys.2018.00214



NanoSIMS image of a cross section of an anemone. In the outer layer are the stinging nematocysts with their coiled barbs (purple). The inner layer contains mainly symbiotic algae (round and pink).

9 SHAPE SHIFTING AT THE NANOSCALE

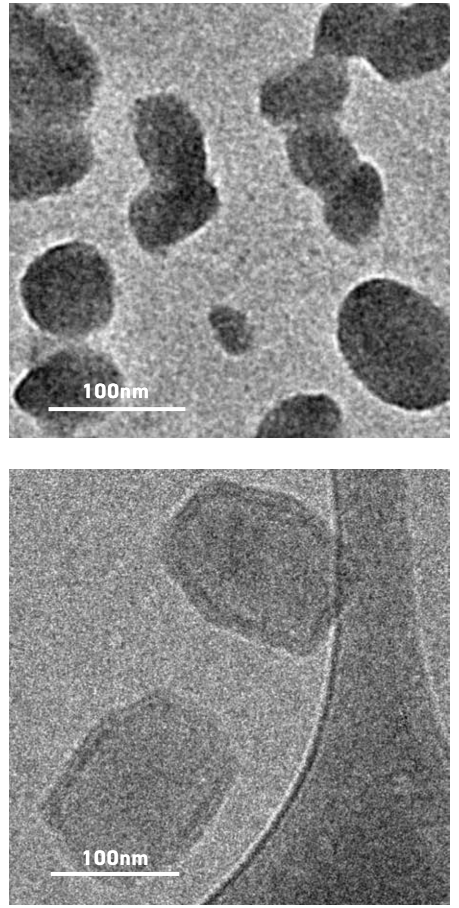
Nanoparticles with custom designed properties are important to various fields of research from mechanical engineering to personalised medicine. Hard metal nanoparticles can be designed and made into a plethora of shapes, but this is much more difficult with soft polymeric nanoparticles.

Soft materials in the nanometere size range are also more difficult to analyse as most of them only reveal their true shape when wet. This means that cryo-electron microscopy, where samples are snap-frozen, is the only feasible technique.

A team of researchers led by Pall Thordarson from UNSW used this approach to show that a perylene-bearing block copolymer can self-assemble into membrane sacs called polymersomes. The researchers showed that these polymersomes spontaneously transition from spheres into unusual faceted polyhedral shapes. They were able to visualise the entire process, uncovering how the shape transformation is driven by the aggregation of perylene as it is confined within a spherical polymersome shell. The team was also able to control the shape transformation process and isolate specific shapes as required.

The particles were also found to be intrinsically fluorescent, an extra feature that could be valuable in tracking them as they are used in a number of different applications. Taking the drug delivery field as an example, the efficiency of nanoparticle uptake into cells has been shown to be highly dependent on the shape of the nanoparticles. These results open opportunities for the use of non-spherical polymersomes for drug delivery, nanoreactor or templating applications.

Ref: Wong CK et al. Chem Sci 2019;10(9);2725, doi: 10.1039/c8sc04206c



Cryo-TEM images of spherical and polyhedral polymersomes.

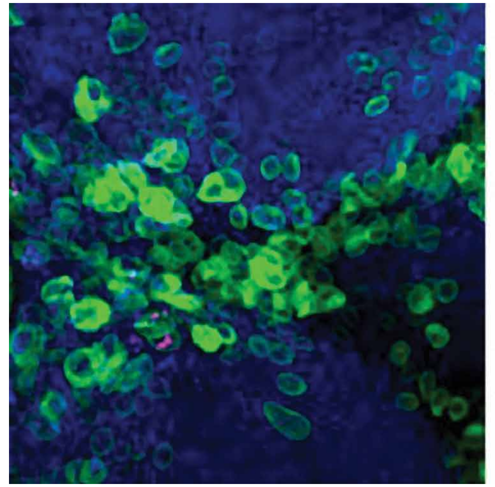
10 ORIGINS OF CHRONIC PAIN

Chronic pain has an enormous impact on the quality of life for billions of people worldwide and is estimated to cost trillions of dollars per year. Despite decades of research, it is still not clear how chronic pain develops, why it prevails, and how best to treat the underlying pathology. In a paper published in the journal *Science Advances*, Dr Thang Khuong and A/Prof. Greg Neely at the University of Sydney report on their in-depth study to investigate the evolution of chronic pain using the fruit fly, *Drosophila*.

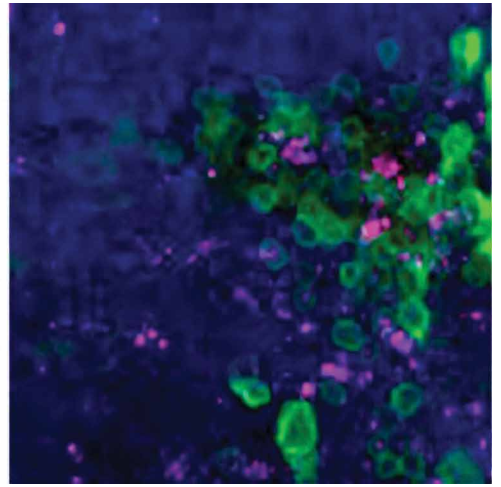
The underlying mechanisms causing chronic "pain" in flies were studied by using a combination of behavioural, genetic and microscopic analyses. They found that pain-killing nerve cells in the insects' ventral nerve cord, the insect equivalent of our spinal cord, were lost. Similar observations have been made in mice and human chronic pain patients. The protein stained pink in the confocal microscopy image (below) of a *Drosophila* "spinal cord" is active caspase, and this is responsible for the loss of those pain killing nerve cells, resulting in neuropathic "pain". These data establish that chronic pain was actually advantageous at some point in evolution, however in modern humans, chronic pain is now a liability.

Now that the core mechanism causing chronic pain has been identified, new therapies targeting the underlying cause of chronic pain are being developed by Neely and his team.

Ref.: Thang M. Khuong et al., 2019. Science Advances, 5 (7), eaaw4099



Confocal image of an uninjured nerve cord.



Confocal image of an injured nerve cord showing active caspase in pink, which kills off the pain-killing nerve cells.

Ventral nerve cord (equivalent to the human spinal cord) of an uninjured fly with the pain nerve cell projections shown in green, pain inhibiting neural transmitters in red and neural synapses in yellow.

CHALLENGE

Australia has a unique and demanding environment with soils that are often extremely low in phosphorus. This presents a challenge for our current suite of crops, almost all of which originated elsewhere and are adapted to different soil types. These crops require significant amounts of fertiliser to enable them to grow in these low phosphorus soils. Understanding how native plants deal with these low levels of phosphorus is providing new strategies to improve efficiency of crop production.

11

NUTRIENT MANAGEMENT – KEY TO SURVIVAL

Images: flower (left) and cone (right) of Banksia menziesii Sophie Xiang

RESEARCH

Southwest Australia is a global biodiversity hotspot where, for example, Banksia and Hakea plant species excel at very low soil and leaf phosphorus concentrations, yet exhibit rates of photosynthesis similar to those of crop plants, which have a much higher demand for phosphorus. How do they do this?

A/Prof. Peta Clode, working with a team of researchers led by E/Prof. Hans Lambers at the University of Western Australia (UWA), used cryo scanning electron microscopy at the UWA Microscopy Australia facility, to determine the concentration of elements in single leaf cells across a range of Australian, South American, and important crop plants. They discovered that higher photosynthetic efficiency is partly achieved by preferentially allocating phosphorus to where it is needed most – in the cells that do the majority of the photosynthesis. Interestingly, species in other families that evolved in phosphorus-impoverished landscapes also show this same phosphorus-efficiency trait. However, species in the same families that evolved in environments with richer soils do not. In the important crop, lupin, they found no preferential allocation of phosphorus to photosynthetic cells across species.

With this, calcium must be adequately separated from the phosphorus-containing cells to avoid precipitation of calcium phosphates, which reduces the availability of these elements to the plant. This work has highlighted that plants that are good at keeping calcium and phosphorus away from each other (i.e. in different types of leaf cells), can tolerate a much wider range of soil calcium and phosphorus conditions.

These results highlight the likely role of soil phosphorus in driving the evolution of ecologically relevant nutrient-allocation patterns and that these patterns cannot be generalised across families as has been previously modelled.

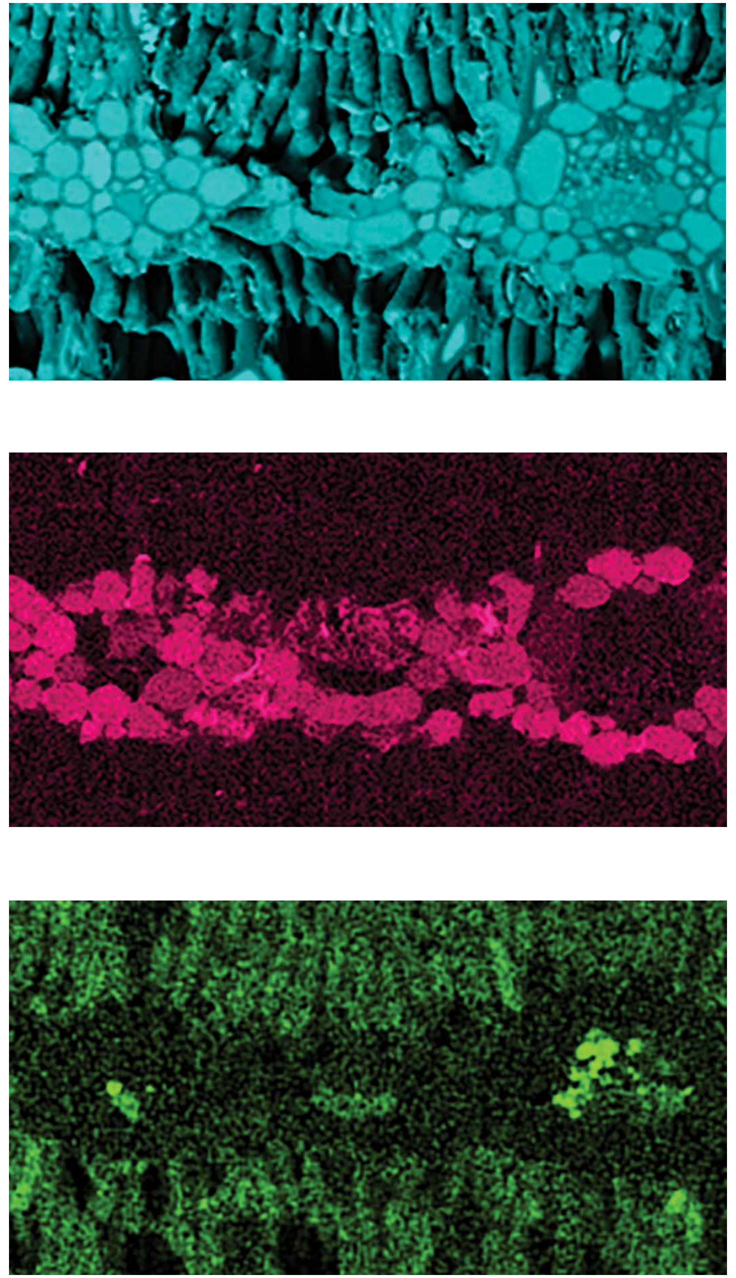
IMPACT

- Better strategies for conserving Australia's floral biodiversity
- New approaches to selecting and breeding crop lineages capable of growing in Australia's low phosphorus soils
- Alleviating issues related to high phosphorus fertiliser use.
- More informed management of Proteaceae in restoration projects and in the horticultural industry

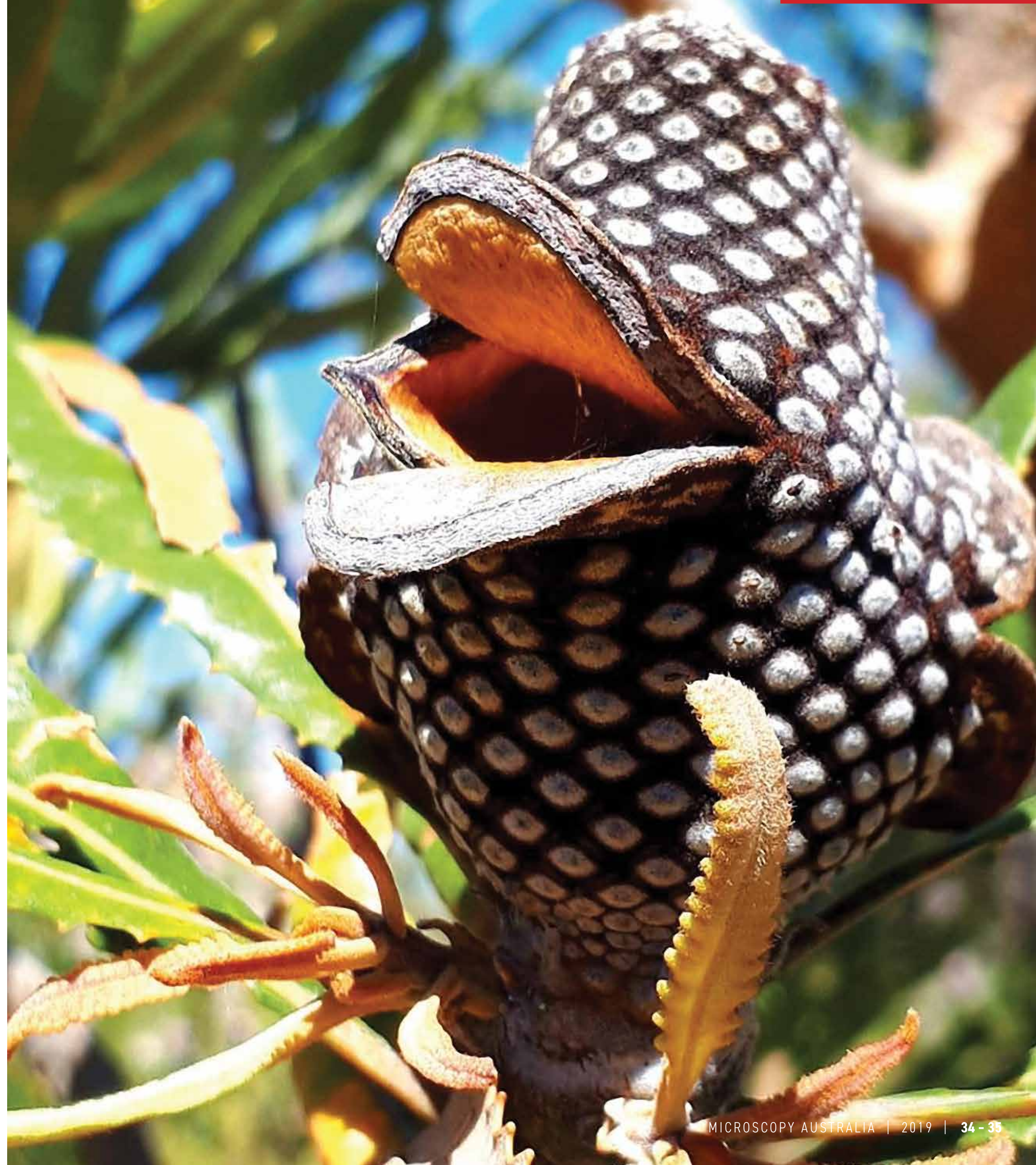
Refs: Ding W. et al., 2018, Plant Cell Environ 41:1512-23.

Guilherme-Pereira C et al., 2018, New Phytol 218:959-73.

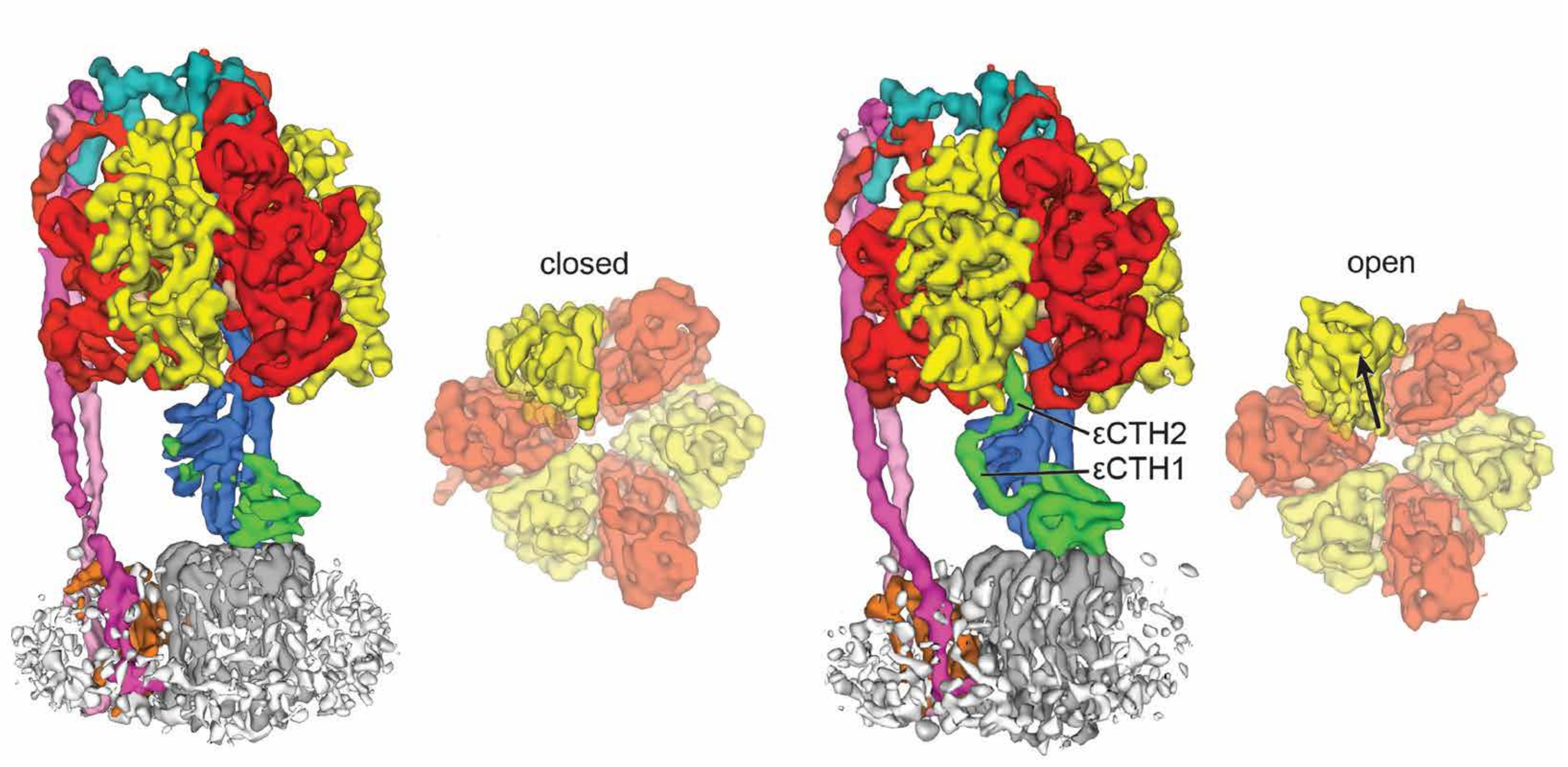
Hayes PE et al., 2018. Plant Cell Environ 41:605-19.



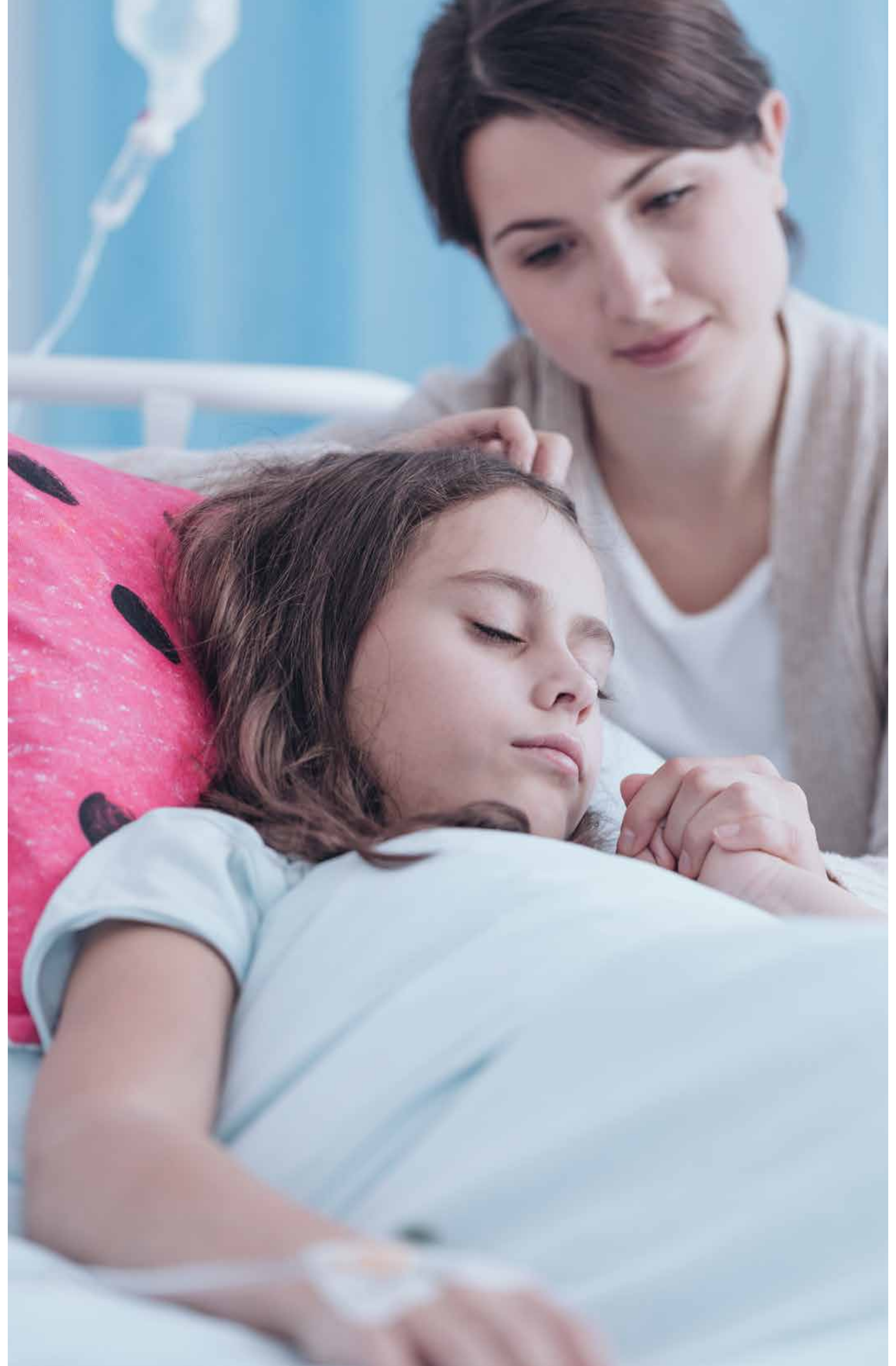
Element maps showing the distribution of oxygen (O) (top), calcium (Ca) (middle) and phosphorus (P) (bottom) in Hakea prostrata exposed to high Ca levels. The O map shows the leaf anatomy. The two rows of palisade mesophyll (photosynthetic cell layers) dark in the Ca map, but high in P.



POTENTIALLY SAVING MILLIONS OF LIVES



Two of the ATP synthase structures determined by the researchers using cryo-TEM.



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BEATING THE BACTERIA

CHALLENGE

With the rise of antibiotic resistance, researchers are constantly seeking new approaches to keep one step ahead in the fight against bacterial infections. Many cellular processes and molecular structures are similar between humans and bacteria but there are differences. These differences are the best targets to explore as they should allow drugs to be developed that are specific to bacteria without interfering with the normal functioning of the humans and animals they aim to protect.

RESEARCH

In cells from bacteria to humans, energy from the metabolism of nutrients is held in a chemical called adenosine triphosphate (ATP). ATP is produced by a protein called ATP synthase, a complex enzyme that rotates like a biological motor to add a phosphate onto adenosine diphosphate (ADP) to make ATP. When energy is needed to power cellular processes, ATP is converted back to ADP by removal of a phosphate group, which releases energy.

ATP synthase uses a rotary catalytic mechanism, whereby rotation of a central axel confers shape changes within the protein that facilitate chemical reactions. Researchers from the Victor Chang Cardiac Research Institute, UNSW Sydney and collaborators in New York and Oxford have now determined the 3D structures of the different shapes that ATP synthase adopts as it carries out different activities. Amongst the various structures, they observed that one is unique to bacteria. This is a region of the protein that can flip into a position that stops the enzyme from functioning. This occurs to save resources when the bacteria are under stress. However, this mechanism could potentially be highjacked by drug designers to switch off the enzyme permanently, killing the bacteria.

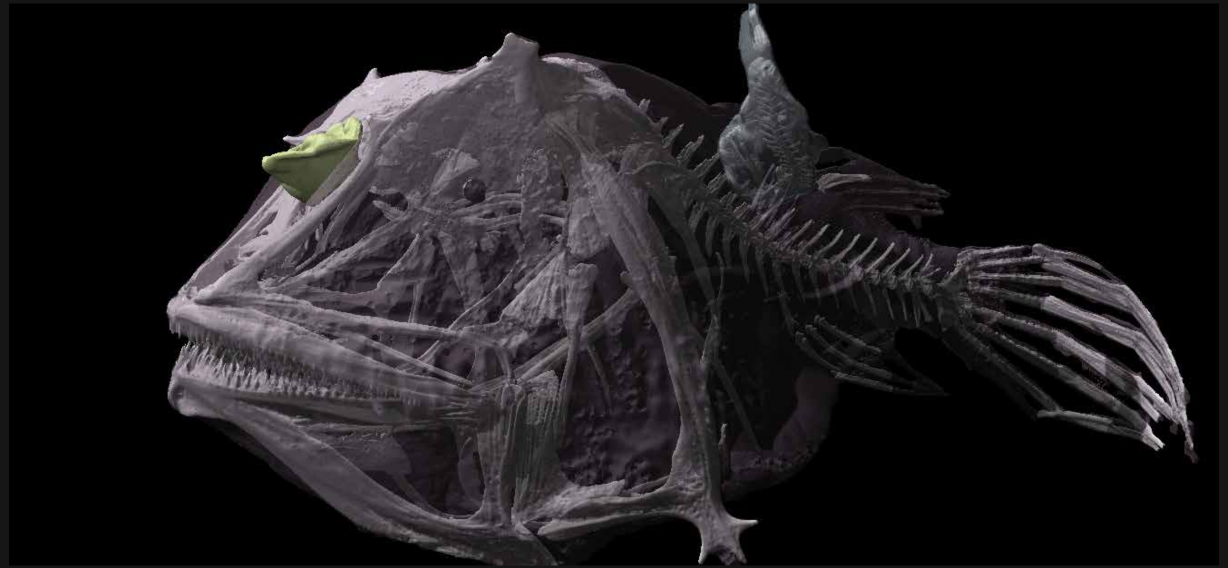
The protein structures revealed by this research are the first to be determined using the recently acquired cryo TEM at the Microscopy Australia facility at UNSW Sydney.

IMPACT

This new knowledge will:

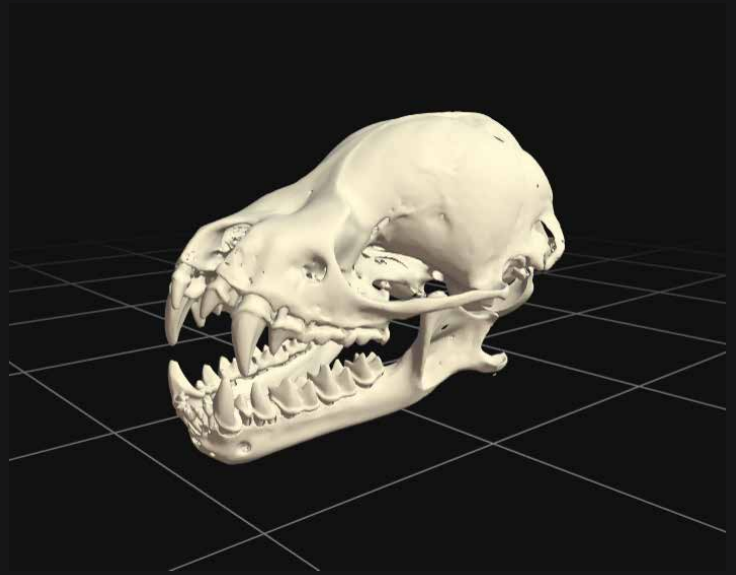
- inform antibacterial drug design, potentially saving millions of lives
- provide insights into potential functional designs for bionanotechnology components.

Ref. M. Sobti et al., 2019, eLife 2019;8:e43864. DOI: https://doi.org/10.7554/eLife.43864



A female Haplophryne mollis, an angler fish with a lure and parasitic male.

Visitors enjoying the Australian Museum displays.



The skull and jaw of a New Caledonian long-eared bat, the holotype from the Australian Museum.

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MUSEUMS LOOK TO THE FUTURE

CHALLENGE

Childhood visits to the natural history museum – full of glowing cabinets carefully arranged with a narrative of biology, evolution, and of course, dinosaurs – can be inspiring. But you only get to see the museum's public display. Only a tiny fraction of the crucially important and irreplaceable objects can be on show, the rest are meticulously stored behind the scenes. While each object has the potential to be an artists' muse, inspiration for an engineer or designer, or provide data for scientists, visitors only see a few. How can more be revealed?

RESEARCH

Microscopy Australia's micro-CT facilities at the Australian National University (ANU) and the University of Western Australia (UWA) are each helping to reveal hidden samples and see inside valuable specimens without damaging them. The Australian Museum in Sydney selects high priority specimens (those in demand for researchers, difficult to assess through photos, challenging to ship, and sometimes specimens on which species are based) and carefully sends them to the CTLab at ANU. There, each specimen is imaged in micro-CT instruments developed at ANU. The data is reconstructed into a 3D volume with interactive surfaces, destined for the Australian Museum's online portal that uses Pedestal, a product produced by Macquarie University. The portal's digital archives will let visitors interact with specimens that would not otherwise be on display.

The Western Australian Museum is also undertaking a similar project, using our Micro-CT facilities at UWA to create full 3D datasets of insects, crustaceans, arachnids and fossil shark teeth that will be turned into interactive digital displays or larger-than-life scale models. Entomology curator Dr Nikolai Tatarnic says "With micro-CT imaging we can bring the microscopic world to life at a scale that people can appreciate."

IMPACT

- Visitors can see the microscopic details of the miniscule creatures that make up most of the animal diversity on the planet, inspiring children and adults with the wonder of science and nature.
- Researchers can visualise previously inaccessible morphological data without destroying precious samples.
- A more complete set of specimens is available for the public to explore
- Virtual samples improve regional access to museums' collections

Occiperipatoides gilesii is a velvet worm from the southwest of WA.

Phaconeura proserpina is a blind, cave-dwelling planthopper from WA.

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Scanning electron micrograph of tantalum crystals | Dr Ben Pace

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